

=> d his ful

(FILE 'HOME' ENTERED AT 11:15:44 ON 06 APR 2006)

FILE 'REGISTRY' ENTERED AT 11:15:51 ON 06 APR 2006

L1 STR

L2 0 SEA SSS SAM L1

L3 2 SEA SSS FUL L1

D SCA

FILE 'HCAPLUS' ENTERED AT 11:21:34 ON 06 APR 2006

L4 1 SEA ABB=ON PLU=ON L3

FILE 'BEILSTEIN' ENTERED AT 11:22:03 ON 06 APR 2006

L5 0 SEA SSS SAM L1

L6 1 SEA SSS FUL L1

L7 1 SEA ABB=ON PLU=ON L6/COM

FILE 'MARPAT' ENTERED AT 11:25:57 ON 06 APR 2006

L8 1 SEA SSS SAM L1

L9 6 SEA SSS FUL L1

L10 2 SEA ABB=ON PLU=ON L9/COM

L\*\*\* DEL 2 S L9/COM

L11 1 SEA ABB=ON PLU=ON L10 NOT L4

FILE 'STNGUIDE' ENTERED AT 11:27:38 ON 06 APR 2006

FILE 'REGISTRY' ENTERED AT 11:37:45 ON 06 APR 2006

L12 STR L1

L\*\*\* DEL 1 S L12

L13 STR L12

L14 1 SEA SSS SAM L13

D SCA

L15 0 SEA ABB=ON PLU=ON C66/ES AND F/ELS

L16 68869 SEA ABB=ON PLU=ON C6-C6/ES AND F/ELS

L17 892571 SEA ABB=ON PLU=ON C6-C6/ES

L18 0 SEA SUB=L17 SSS SAM L12

L19 142 SEA SUB=L17 SSS FUL L12

FILE 'HCAPLUS' ENTERED AT 11:44:04 ON 06 APR 2006

L20 468 SEA ABB=ON PLU=ON L19

S L13

FILE 'REGISTRY' ENTERED AT 11:44:30 ON 06 APR 2006

L21 3 SEA SUB=L19 SSS SAM L13

FILE 'HCAPLUS' ENTERED AT 11:44:30 ON 06 APR 2006

L22 2 SEA ABB=ON PLU=ON L21

FILE 'REGISTRY' ENTERED AT 11:44:36 ON 06 APR 2006

L23 3 SEA SUB=L19 SSS SAM L13

L24 142 SEA SUB=L19 SSS FUL L13

FILE 'HCAPLUS' ENTERED AT 11:45:41 ON 06 APR 2006

L25 468 SEA ABB=ON PLU=ON L24

FILE 'STNGUIDE' ENTERED AT 11:45:52 ON 06 APR 2006

FILE 'REGISTRY' ENTERED AT 11:55:25 ON 06 APR 2006

L26 STR  
L27 0 SEA SUB=L24 SSS SAM L26  
L28 22 SEA SUB=L24 SSS FUL L26

FILE 'HCAPLUS' ENTERED AT 12:12:26 ON 06 APR 2006  
L29 466 SEA ABB=ON PLU=ON L28  
L30 ANALYZE PLU=ON L25 1-468 RN : 8943 TERMS  
D

FILE 'REGISTRY' ENTERED AT 12:13:34 ON 06 APR 2006  
L31 1 SEA ABB=ON PLU=ON 116644-53-2  
D SCA  
L32 141 SEA ABB=ON PLU=ON L24 NOT L31

FILE 'HCAPLUS' ENTERED AT 12:14:05 ON 06 APR 2006  
L33 71 SEA ABB=ON PLU=ON L32  
L34 50 SEA ABB=ON PLU=ON L28 NOT L31

FILE 'REGISTRY' ENTERED AT 12:14:25 ON 06 APR 2006  
L35 21 SEA ABB=ON PLU=ON L28 NOT L31

FILE 'HCAPLUS' ENTERED AT 12:14:32 ON 06 APR 2006  
L36 69 SEA ABB=ON PLU=ON L35  
L37 ANALYZE PLU=ON L36 1-69 RN : 4177 TERMS  
D

FILE 'REGISTRY' ENTERED AT 12:16:04 ON 06 APR 2006  
L38 1 SEA ABB=ON PLU=ON 116666-63-8  
L39 20 SEA ABB=ON PLU=ON L35 NOT L38

FILE 'HCAPLUS' ENTERED AT 12:16:18 ON 06 APR 2006  
L40 13 SEA ABB=ON PLU=ON L39  
L41 416 SEA ABB=ON PLU=ON L31  
L42 63 SEA ABB=ON PLU=ON L38

## FILE HOME

## FILE REGISTRY

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 4 APR 2006 HIGHEST RN 879269-14-4  
DICTIONARY FILE UPDATES: 4 APR 2006 HIGHEST RN 879269-14-4

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH January 6, 2006

Please note that search-term pricing does apply when conducting SmartSELECT searches.

\*\*\*\*\*

\* The CA roles and document type information have been removed from \*  
\* the IDE default display format and the ED field has been added, \*  
\* effective March 20, 2005. A new display format, IDERL, is now \*  
\* available and contains the CA role and document type information. \*

\*\*\*\*\*

Structure search iteration limits have been increased. See HELP SLIMITS for details.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

<http://www.cas.org/ONLINE/UG/regprops.html>

FILE HCPLUS

Copyright of the articles to which records in this database refer is held by the publishers listed in the PUBLISHER (PB) field (available for records published or updated in Chemical Abstracts after December 26, 1996), unless otherwise indicated in the original publications. The CA Lexicon is the copyrighted intellectual property of the American Chemical Society and is provided to assist you in searching databases on STN. Any dissemination, distribution, copying, or storing of this information, without the prior written consent of CAS, is strictly prohibited.

FILE COVERS 1907 - 6 Apr 2006 VOL 144 ISS 15  
FILE LAST UPDATED: 4 Apr 2006 (20060404/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE BEILSTEIN  
FILE LAST UPDATED ON MARCH 15, 2006

FILE COVERS 1771 TO 2006.  
FILE CONTAINS 9,516,393 SUBSTANCES

>>> PLEASE NOTE: Reaction Data and substance data are stored in separate documents and can not be searched together in one query. Reaction data for BEILSTEIN compounds may be displayed immediately with the display codes PRE (preparations) and REA (reactions). A substance answer set retrieved after the search for a chemical name, a compounds with available reaction information by combining with PRE/FA, REA/FA or more generally with RX/FA. The BEILSTEIN Registry Number (BRN) is the link between a BEILSTEIN compound and belonging reactions. For more detailed reaction searches BRNs can be searched as reaction partner BRNs Reactant BRN (RX.RBRN) or Product BRN (RX.PBRN).<<<

>>> FOR SEARCHING PREPARATIONS SEE HELP PRE <<<

\*\*\*\*\*  
\* PLEASE NOTE THAT THERE ARE NO FORMATS FREE OF COST. \*  
\* SET NOTICE FEATURE: THE COST ESTIMATES CALCULATED FOR SET NOTICE \*  
\* ARE BASED ON THE HIGHEST PRICE CATEGORY. THEREFORE; THESE \*  
\* ESTIMATES MAY NOT REFLECT THE ACTUAL COSTS. \*  
\* FOR PRICE INFORMATION SEE HELP COST \*  
\*\*\*\*\*

## NEW

- \* PATENT NUMBERS (PN) AND BABS ACCESSION NUMBERS (BABSAN) CAN NOW BE SEARCHED, SELECTED AND TRANSFERRED.
- \* NEW DISPLAY FORMATS ALLREF, ALLP AND BABSAN SHOW ALL REFERENCES, ALL PATENT REFERENCES, OR ALL BABS ACCESSION NUMBERS FOR A COMPOUND AT A GLANCE.

FILE MARPAT

FILE CONTENT: 1961-PRESENT VOL 144 ISS 14 (20060331/ED)

SOME MARPAT RECORDS ARE DERIVED FROM INPI DATA FOR 1961-1987

MOST RECENT CITATIONS FOR PATENTS FROM MAJOR ISSUING AGENCIES (COVERAGE TO THESE DATES IS NOT COMPLETE):

US	2006035965	16 FEB 2006
DE	102004039876	26 JAN 2006
EP	1621541	01 FEB 2006
JP	2006045074	16 FEB 2006
WO	2006012333	02 FEB 2006
GB	2416167	18 JAN 2006
FR	2874013	10 FEB 2006
RU	2267521	10 JAN 2006
CA	2512063	14 JAN 2006

Expanded G-group definition display now available.

New CAS Information Use Policies, enter HELP USAGETERMS for details.

FILE STNGUIDE

FILE CONTAINS CURRENT INFORMATION.

LAST RELOADED: Mar 31, 2006 (20060331/UP).

=> fil hcap

FILE 'HCAPLUS' ENTERED AT 12:30:32 ON 06 APR 2006

USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.

PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

COPYRIGHT (C) 2006 AMERICAN CHEMICAL SOCIETY (ACS)

Copyright of the articles to which records in this database refer is held by the publishers listed in the PUBLISHER (PB) field (available for records published or updated in Chemical Abstracts after December 26, 1996), unless otherwise indicated in the original publications.

The CA Lexicon is the copyrighted intellectual property of the American Chemical Society and is provided to assist you in searching databases on STN. Any dissemination, distribution, copying, or storing of this information, without the prior written consent of CAS, is strictly prohibited.

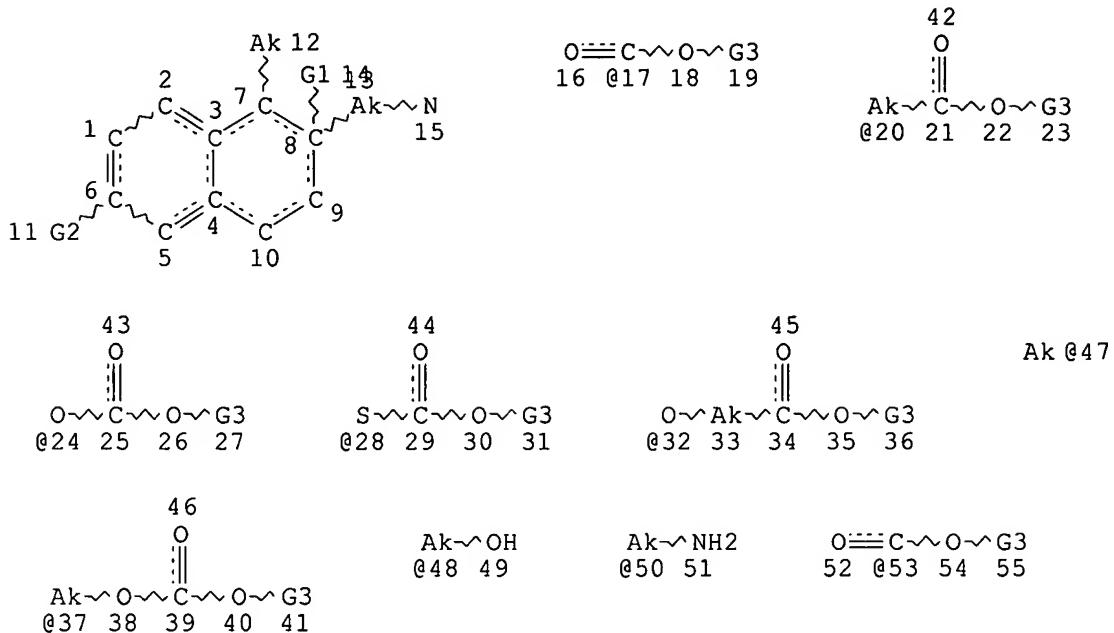
FILE COVERS 1907 - 6 Apr 2006 VOL 144 ISS 15

FILE LAST UPDATED: 4 Apr 2006 (20060404/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d que stat 14  
L1 STR



VAR G1=17/20/24/28/32/37

VAR G2=X/53

VAR G3=47/48/50

NODE ATTRIBUTES:

CONNECT IS E3 RC AT 7

CONNECT IS E1 RC AT 12

CONNECT IS E3 RC AT 15

CONNECT IS E2 RC AT 20

CONNECT IS E2 RC AT 33

CONNECT IS E2 RC AT 37

CONNECT IS E1 RC AT 47

DEFAULT MLEVEL IS ATOM

GGCAT IS LOC AT 12

GGCAT IS LIN SAT AT 20

GGCAT IS LIN SAT AT 33

GGCAT IS LIN SAT AT 37

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 55

STEREO ATTRIBUTES: NONE

L3 2 SEA FILE=REGISTRY SSS FUL L1

L4 1 SEA FILE=HCAPLUS ABB=ON PLU=ON L3

=> d 14 ibib abs hitstr

L4 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1987:49807 HCAPLUS

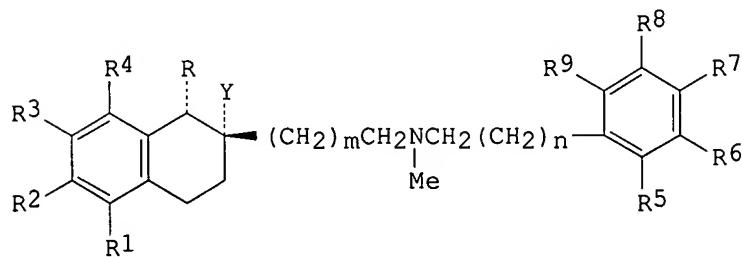
DOCUMENT NUMBER: 106:49807

TITLE: Tetrahydronaphthalene derivatives, their

INVENTOR(S): intermedicates, and medicines containing them  
 Hengartner, Urs; Ramuz, Henri  
 PATENT ASSIGNEE(S): Hoffmann-La Roche, F., und Co. A.-G., Fed. Rep. Ger.  
 SOURCE: Eur. Pat. Appl., 53 pp.  
 CODEN: EPXXDW  
 DOCUMENT TYPE: Patent  
 LANGUAGE: German  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 177960	A2	19860416	EP 1985-112863	19851010
EP 177960	A3	19880113		
EP 177960	B1	19910320		
R: AT, BE, CH, FI 8503817	DE, FR, GB, IT, LI, LU, NL, SE			
FI 83508	A	19860412	FI 1985-3817	19851002
FI 83508	B	19910415		
FI 83508	C	19910725		
AU 8548301	A1	19860417	AU 1985-48301	19851004
AU 589375	B2	19891012		
ZA 8507681	A	19860528	ZA 1985-7681	19851004
IL 76576	A1	19890131	IL 1985-76576	19851004
JP 61091157	A2	19860509	JP 1985-222893	19851008
HU 38605	A2	19860630	HU 1985-3915	19851009
HU 199773	B	19900328		
CN 85107496	A	19860723	CN 1985-107496	19851009
CN 1007727	B	19900425		
CA 1287636	A1	19910813	CA 1985-492588	19851009
DK 8504648	A	19860412	DK 1985-4648	19851010
NO 8504036	A	19860414	NO 1985-4036	19851010
NO 161971	B	19890710		
NO 161971	C	19891018		
ES 547756	A1	19861116	ES 1985-547756	19851010
US 4680310	A	19870714	US 1985-786253	19851010
AT 61791	E	19910415	AT 1985-112863	19851010
ES 554021	A1	19871216	ES 1986-554021	19860416
ES 554020	A1	19880516	ES 1986-554020	19860416
PRIORITY APPLN. INFO.:			CH 1984-4870	A 19841011
			EP 1985-112863	A 19851010

OTHER SOURCE(S): MARPAT 106:49807  
 GI



I

AB Tetrahydronaphthalene derivs. I [R = H, alkyl; R1-R4 = H, halo, alkoxy, etc.; R5-R9 = H, halo, C1-10 alkoxy, alkylthio,  $\omega,\omega,\omega$ -trifluoroalkoxy, etc.; Y = OH, alkylcarbonyloxy, alkoxyalkylcarbonyloxy,

alkoxycarbonyloxy, alkoxyalkoxycarbonyloxy, alkylthioalkylcarbonyloxy, (un)substituted benzylcarbonyloxy;  $m = 1, 2$ ;  $n = 1, 2, 3$ ] in racemates and optical antipodes, having Ca-antagonistic and antiarrhythmic effects, are prepared. Thus, 2-(p-fluorophenyl)-3-methylbutyric acid was converted to the acid chloride and treated with ethylene in the presence of  $AlCl_3$  to give 6-fluoro-3,4-dihydro-1-isopropyl-2(1H)-naphthalenone, which underwent Grignard reaction with  $BrCH_2CO_2CMe_3$ , followed by reduction with  $LiAlH_4$ , to give 6-fluoro-1,2,3,4-tetrahydro-2-hydroxy-1 $\alpha$ -isopropyl-2 $\beta$ -naphthalenylethanol. This intermediate was tosylated, condensed with N-methylhomoveratrylamine, and acylated with methoxyacetyl chloride to give 2-[2-[(3,4-dimethoxyphenylethyl)methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1 $\alpha$ -isopropyl-2 $\alpha$ -naphthyl methoxyacetate-HCl (II).

II was tested for Ca-antagonistic and hypotensive effects. A tablet was formulated containing II 75, lactose 135, starch 70, Povidone K 15, talc 3, and Mg stearate 2 mg.

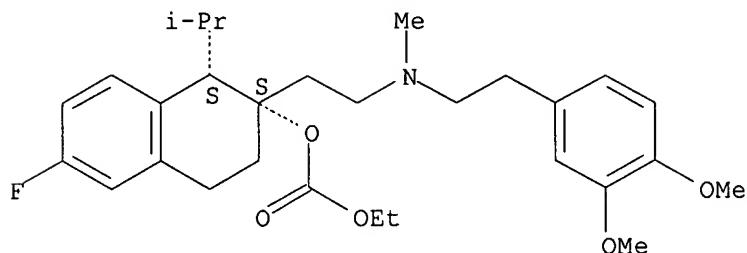
IT 104205-35-8P 104221-42-3P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(preparation of, as calcium antagonist)

BN 104205-35-8 HCAPLUS

KN 101205-33-0 NCI-CHEM  
CN Carbonic acid, 2-[2-[(2-(3,4-dimethoxyphenyl)ethyl)methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl ethyl ester, hydrochloride, cis- (9CI) (CA INDEX NAME)

### Relative stereochemistry.

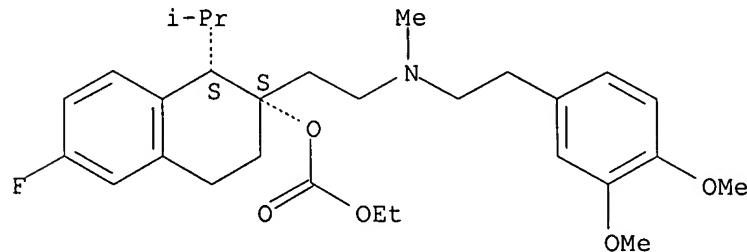


• HCl

RN 104221-42-3 HCAPLUS

CN Carbonic acid, 2-[2-[(2-(3,4-dimethoxyphenyl)ethyl)methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl ethyl ester, cis- (9CI) (CA INDEX NAME)

## Relative stereochemistry.



```
=> fil beilst
```

FILE 'BEILSTEIN' ENTERED AT 12:30:50 ON 06 APR 2006

COPYRIGHT (c) 2006 Beilstein-Institut zur Foerderung der Chemischen Wissenschaften  
licensed to Beilstein GmbH and MDL Information Systems GmbH

FILE LAST UPDATED ON MARCH 15, 2006

FILE COVERS 1771 TO 2006.

\*\*\* FILE CONTAINS 9,516,393 SUBSTANCES \*\*\*

>>> PLEASE NOTE: Reaction Data and substance data are stored in separate documents and can not be searched together in one query. Reaction data for BEILSTEIN compounds may be displayed immediately with the display codes PRE (preparations) and REA (reactions). A substance answer set retrieved after the search for a chemical name, a compounds with available reaction information by combining with PRE/FA, REA/FA or more generally with RX/FA. The BEILSTEIN Registry Number (BRN) is the link between a BEILSTEIN compound and belonging reactions. For more detailed reaction searches BRNs can be searched as reaction partner BRNs Reactant BRN (RX.RBRN) or Product BRN (RX.PBRN).<<<

>>> FOR SEARCHING PREPARATIONS SEE HELP PRE <<<

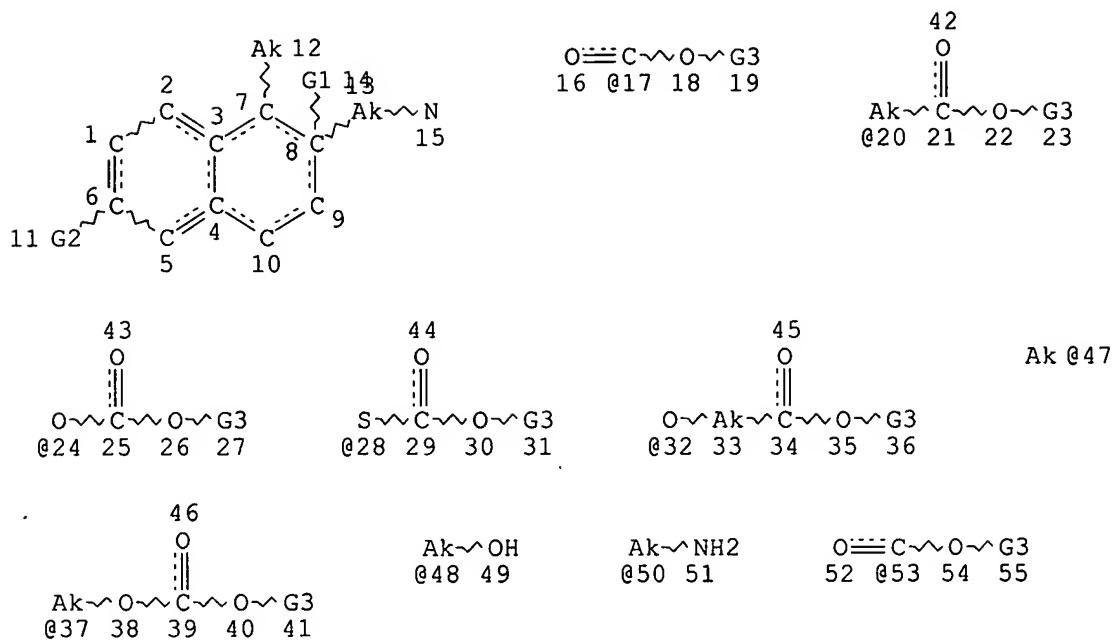
```
*****  
* PLEASE NOTE THAT THERE ARE NO FORMATS FREE OF COST. *  
* SET NOTICE FEATURE: THE COST ESTIMATES CALCULATED FOR SET NOTICE *  
* ARE BASED ON THE HIGHEST PRICE CATEGORY. THEREFORE; THESE *  
* ESTIMATES MAY NOT REFLECT THE ACTUAL COSTS. *  
* FOR PRICE INFORMATION SEE HELP COST *  
*****
```

NEW

```
* PATENT NUMBERS (PN) AND BABS ACCESSION NUMBERS (BABSAN) CAN NOW BE  
SEARCHED, SELECTED AND TRANSFERRED.  
* NEW DISPLAY FORMATS ALLREF, ALLP AND BABSAN SHOW ALL REFERENCES,  
ALL PATENT REFERENCES, OR ALL BABS ACCESSION NUMBERS FOR A  
COMPOUND AT A GLANCE.
```

```
=> d que stat 17
```

L1 STR



VAR G1=17/20/24/28/32/37

VAR G2=X/53

VAR G3=47/48/50

NODE ATTRIBUTES:

CONNECT IS E3 RC AT 7  
 CONNECT IS E1 RC AT 12  
 CONNECT IS E3 RC AT 15  
 CONNECT IS E2 RC AT 20  
 CONNECT IS E2 RC AT 33  
 CONNECT IS E2 RC AT 37  
 CONNECT IS E1 RC AT 47  
 DEFAULT MLEVEL IS ATOM  
 GGCAT IS LOC AT 12  
 GGCAT IS LIN SAT AT 20  
 GGCAT IS LIN SAT AT 33  
 GGCAT IS LIN SAT AT 37  
 DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 55

STEREO ATTRIBUTES: NONE

L6 1 SEA FILE=BEILSTEIN SSS FUL L1  
 L7 1 SEA FILE=BEILSTEIN ABB=ON PLU=ON L6/COM

&gt; d 17 ide allref

L7 ANSWER 1 OF 1 BEILSTEIN COPYRIGHT 2006 BEILSTEIN MDL on STN

Beilstein Records (BRN): 8180430  
 Chemical Name (CN): RO-40-5967  
 Autonom Name (AUN): carbonic acid 2-(2-<<3-(1H-benzoimidazol-2-

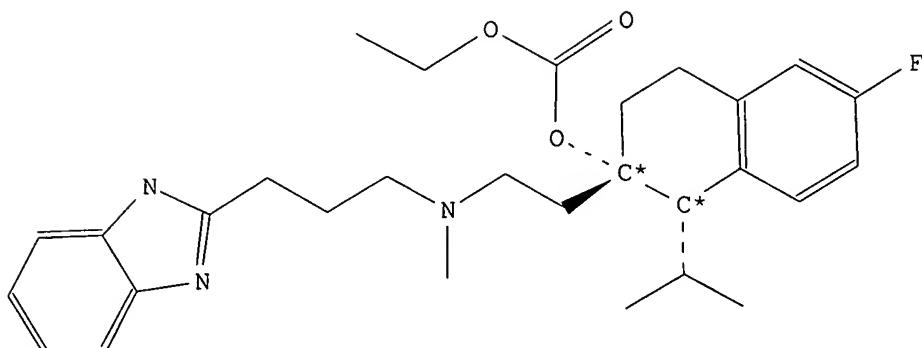
yl)-propyl->-methyl-amino->-ethyl)-6-fluoro-  
 1-isopropyl-1,2,3,4-tetrahydro-naphthalen-  
 2-yl ester ethyl ester; compound with  
 GENERIC INORGANIC NEUTRAL COMPONENT

Fragn. Molec. Formula (FMF): C29 H38 F N3 O3 , Cl H  
 Molecular Formula (MF): C29 H38 F N3 O3 . 2 Cl H  
 Molecular Weight (MW): 495.64, 36.46  
 Fragment BRN (FBRN): 8173779, 1098214  
 Lawson Number (LN): 29577, 15006, 2817, 1762, 298  
 File Segment (FS): Stereo compound  
 Compound Type (CTYPE): heterocyclic  
 Constitution ID (CONSID): 6958260  
 Tautomer ID (TAUTID): 7721684  
 Entry Date (DED): 2000/02/26  
 Update Date (DUPD): 2000/02/26

CM 1

FBRN 8173779

FMF C29 H38 F N3 O3



CM 2

FBRN 1098214

FMF Cl H

## Field Availability:

Code	Name	Occurrence
BRN	Beilstein Records	1
CN	Chemical Name	1
AUN	Autonomname	1
FMF	Fragment Molecular Formula	2
MF	Molecular Formula	1
FW	Formular Weight	2
FBRN	Fragment BRN	2
LN	Lawson Number	5
FS	File Segment	1
CTYPE	Compound Type	1
CONSID	Constitution ID	1

TAUTID	Tautomer ID	1
DED	Entry Date	1
DUPD	Update Date	1
PHARM	Pharmacological Data	1

All References:  
ALLREF

1. Rutledge, Aleta; Triggle, David J., Eur.J.Pharmacol., CODEN: EJPHAZ, 280(2), <1995>, 155 - 158; BABS-6131105

=> fil marpat  
FILE 'MARPAT' ENTERED AT 12:31:16 ON 06 APR 2006  
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.  
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.  
COPYRIGHT (C) 2006 American Chemical Society (ACS)

FILE CONTENT: 1961-PRESENT VOL 144 ISS 14 (20060331/ED)

SOME MARPAT RECORDS ARE DERIVED FROM INPI DATA FOR 1961-1987

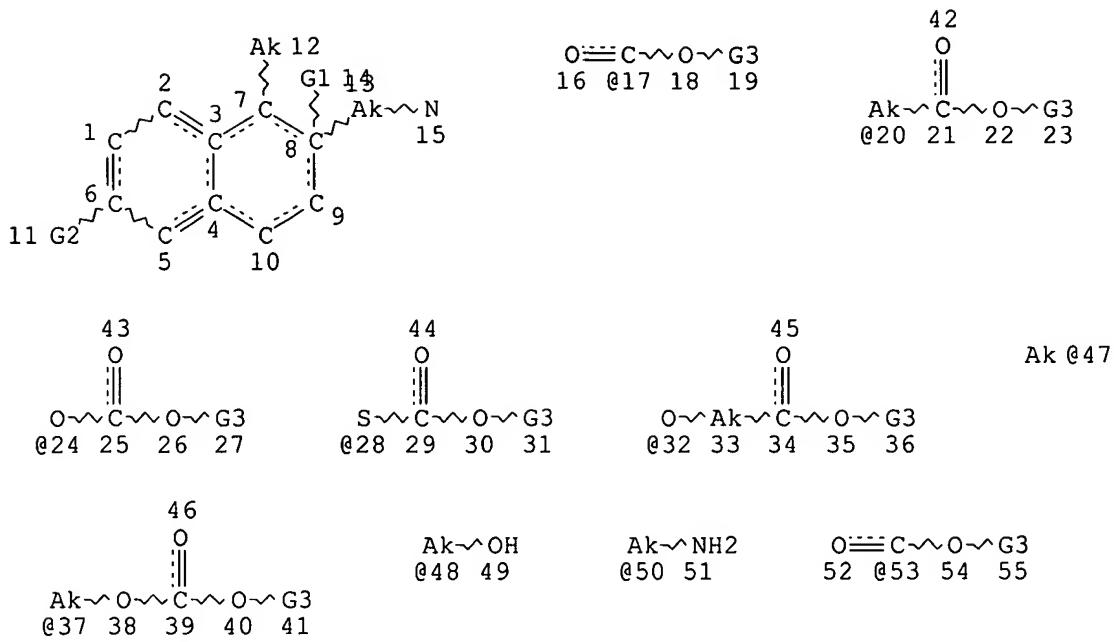
MOST RECENT CITATIONS FOR PATENTS FROM MAJOR ISSUING AGENCIES  
(COVERAGE TO THESE DATES IS NOT COMPLETE):

US	2006035965	16 FEB 2006
DE	102004039876	26 JAN 2006
EP	1621541	01 FEB 2006
JP	2006045074	16 FEB 2006
WO	2006012333	02 FEB 2006
GB	2416167	18 JAN 2006
FR	2874013	10 FEB 2006
RU	2267521	10 JAN 2006
CA	2512063	14 JAN 2006

Expanded G-group definition display now available.

New CAS Information Use Policies, enter HELP USAGETERMS for details.

=> d que stat 111  
L1 STR



VAR G1=17/20/24/28/32/37

VAR G2=X/53

VAR G3=47/48/50

## NODE ATTRIBUTES:

CONNECT IS E3 RC AT 7  
 CONNECT IS E1 RC AT 12  
 CONNECT IS E3 RC AT 15  
 CONNECT IS E2 RC AT 20  
 CONNECT IS E2 RC AT 33  
 CONNECT IS E2 RC AT 37  
 CONNECT IS E1 RC AT 47  
 DEFAULT MLEVEL IS ATOM  
 GGCAT IS LOC AT 12  
 GGCAT IS LIN SAT AT 20  
 GGCAT IS LIN SAT AT 33  
 GGCAT IS LIN SAT AT 37  
 DEFAULT ECLEVEL IS LIMITED

## GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED  
 NUMBER OF NODES IS 55

## STEREO ATTRIBUTES: NONE

L3 2 SEA FILE=REGISTRY SSS FUL L1  
 L4 1 SEA FILE=HCAPLUS ABB=ON PLU=ON L3  
 L9 6 SEA FILE=MARPAT SSS FUL L1  
 L10 2 SEA FILE=MARPAT ABB=ON PLU=ON L9/COM  
 L11 1 SEA FILE=MARPAT ABB=ON PLU=ON L10 NOT L4

=&gt; d 111 ibib abs qhit

L11 ANSWER 1 OF 1 MARPAT COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 138:297661 MARPAT

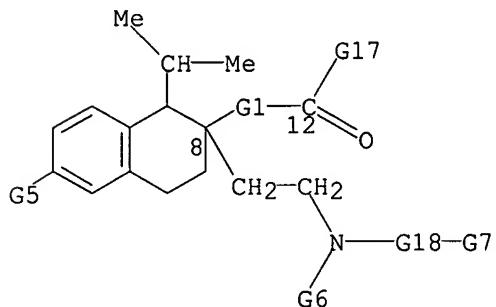
TITLE: Mibepradil-based compounds as calcium channel blockers

useful in the treatment of hypertension and angina  
 INVENTOR(S): Druzgala, Pascal; Milner, Peter G.; Pfister, Jurg R.;  
 Zhang, Xiaoming  
 PATENT ASSIGNEE(S): Aryx Therapeutics, USA  
 SOURCE: PCT Int. Appl., 50 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English

=> l11 qhit  
 L11 IS NOT A RECOGNIZED COMMAND  
 The previous command name entered was not recognized by the system.  
 For a list of commands available to you in the current file, enter  
 "HELP COMMANDS" at an arrow prompt (=>).

=> d 111 qhit  
 L11 ANSWER 1 OF 1 MARPAT COPYRIGHT 2006 ACS on STN

**MSTR 1**



G1 = bond  
 G3 = Me  
 G5 = F  
 G17 = 70



Patent location: claim 2  
 Note: substitution is restricted

=> d 111 ibib abs qhit

L11 ANSWER 1 OF 1 MARPAT COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 138:297661 MARPAT  
 TITLE: Mibepradil-based compounds as calcium channel blockers  
 useful in the treatment of hypertension and angina  
 INVENTOR(S): Druzgala, Pascal; Milner, Peter G.; Pfister, Jurg R.;  
 Zhang, Xiaoming  
 PATENT ASSIGNEE(S): Aryx Therapeutics, USA

SOURCE: PCT Int. Appl., 50 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English

=> fil hcap  
FILE 'HCAPLUS' ENTERED AT 12:32:37 ON 06 APR 2006  
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.  
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.  
COPYRIGHT (C) 2006 AMERICAN CHEMICAL SOCIETY (ACS)

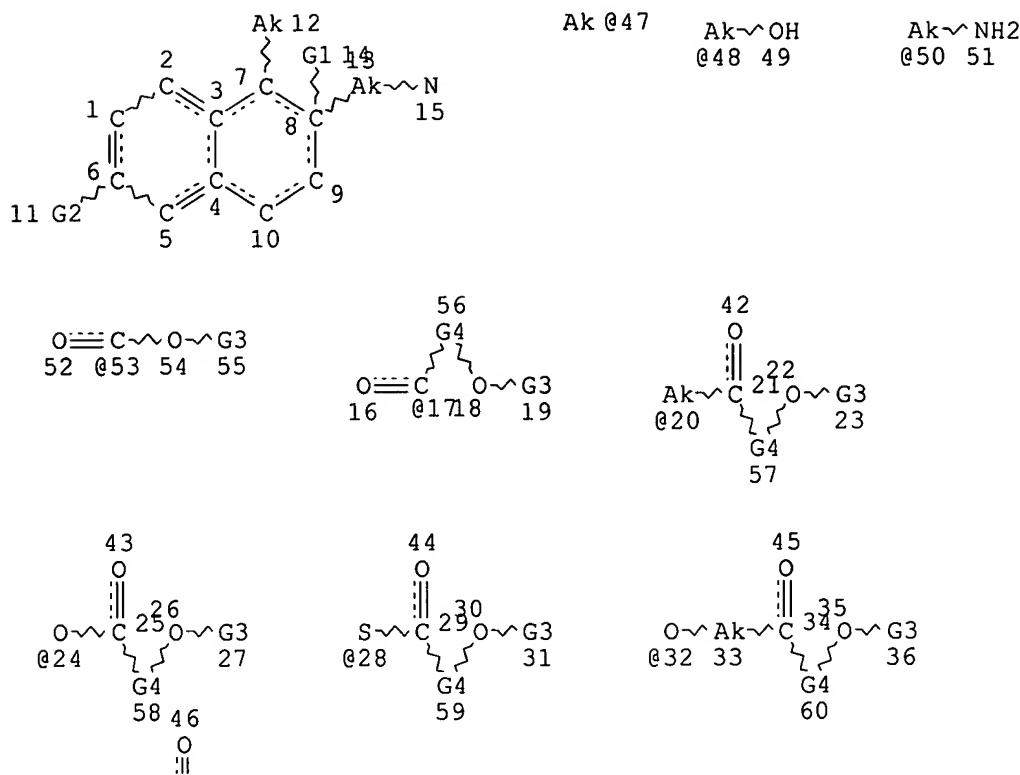
Copyright of the articles to which records in this database refer is held by the publishers listed in the PUBLISHER (PB) field (available for records published or updated in Chemical Abstracts after December 26, 1996), unless otherwise indicated in the original publications. The CA Lexicon is the copyrighted intellectual property of the American Chemical Society and is provided to assist you in searching databases on STN. Any dissemination, distribution, copying, or storing of this information, without the prior written consent of CAS, is strictly prohibited.

FILE COVERS 1907 - 6 Apr 2006 VOL 144 ISS 15  
FILE LAST UPDATED: 4 Apr 2006 (20060404/ED)

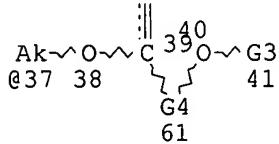
New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d que stat 140  
L12 STR



Page 1-A



Page 2-A

VAR G1=17/20/24/28/32/37

VAR G2=X/53

VAR G3=47/48/50

REP G4=(0-3) CH2

NODE ATTRIBUTES:

CONNECT IS E3 RC AT 7

CONNECT IS E1 RC AT 12

CONNECT IS E3 RC AT 15

CONNECT IS E2 RC AT 20

CONNECT IS E2 RC AT 33

CONNECT IS E2 RC AT 37

CONNECT IS E1 RC AT 47

DEFAULT MLEVEL IS ATOM

GGCAT IS LOC AT 12

GGCAT IS LIN SAT AT 20

GGCAT IS LIN SAT AT 33

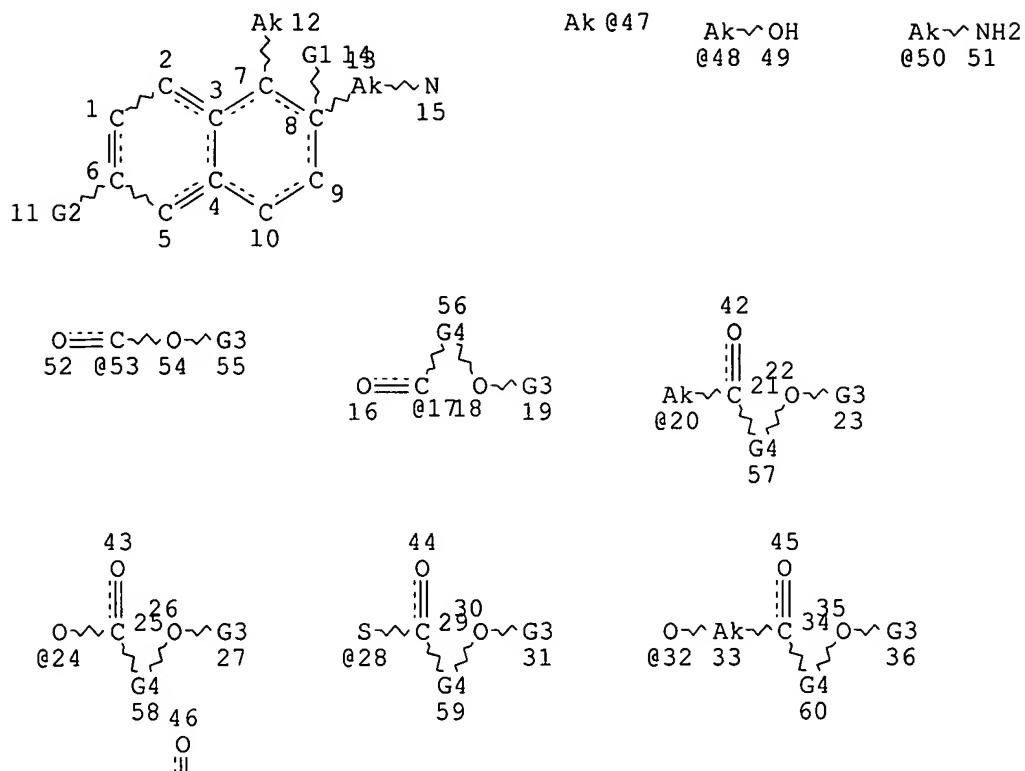
GGCAT IS LIN SAT AT 37

DEFAULT ECLEVEL IS LIMITED

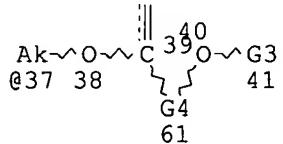
GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 61

STEREO ATTRIBUTES: NONE  
L13 STR

Page 1-A



Page 2-A

VAR G1=17/20/24/28/32/37

VAR G2=X/53

VAR G3=47/48/50

REP G4=(0-1) CH2

NODE ATTRIBUTES:

```

CONNECT IS E3  RC AT    7
CONNECT IS E1  RC AT   12
CONNECT IS E3  RC AT   15
CONNECT IS E2  RC AT   20
CONNECT IS E2  RC AT   33
CONNECT IS E2  RC AT   37
CONNECT IS E1  RC AT  47
DEFAULT MLEVEL IS ATOM
GGCAT  IS LOC  AT   12
GGCAT  IS LIN  SAT  AT   20
GGCAT  IS LIN  SAT  AT   33
GGCAT  IS LIN  SAT  AT   37

```

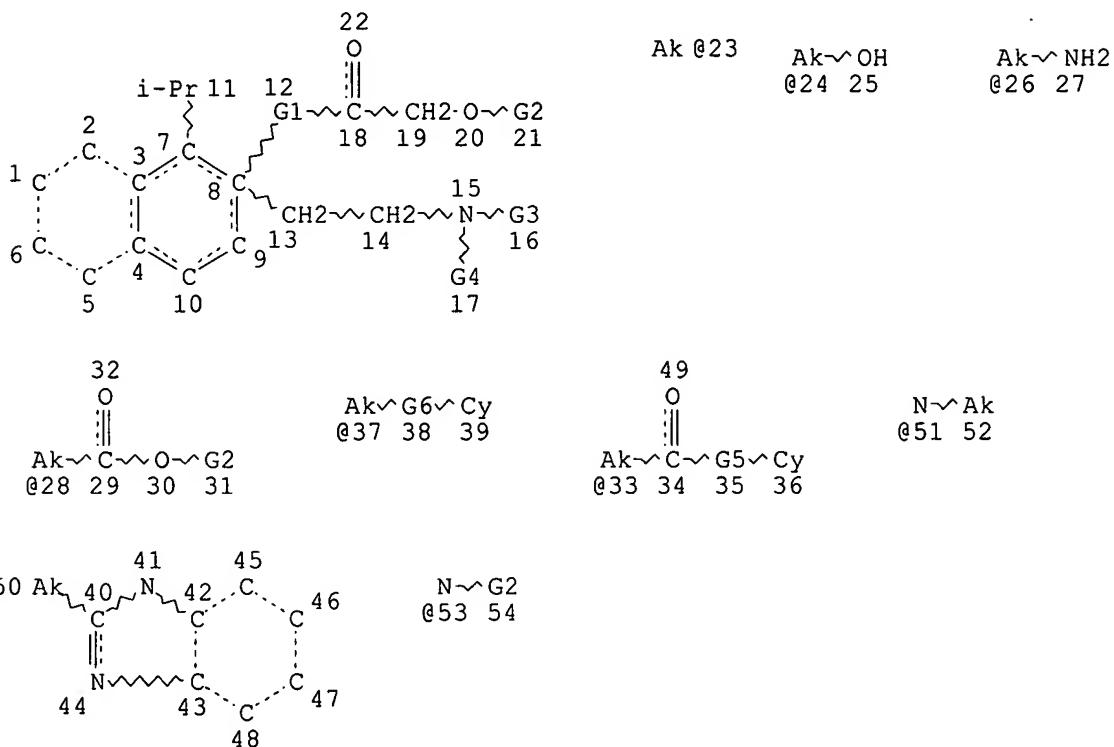
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED  
NUMBER OF NODES IS 61

STEREO ATTRIBUTES: NONE

L17 892571 SEA FILE=REGISTRY ABB=ON PLU=ON C6-C6/ES  
L19 142 SEA FILE=REGISTRY SUB=L17 SSS FUL L12  
L24 142 SEA FILE=REGISTRY SUB=L19 SSS FUL L13  
L26 STR



REP G1=(0-6) A

VAR G2=23/24/26

VAR G3=ME/28

VAR G4=33/37/50

VAR G5=O/NH/51

VAR G6=O/S/NH/53

NODE ATTRIBUTES:

CONNECT IS E1 RC AT 23  
CONNECT IS E2 RC AT 28  
CONNECT IS E2 RC AT 33  
CONNECT IS E2 RC AT 37  
CONNECT IS E2 RC AT 41  
CONNECT IS E2 RC AT 50  
CONNECT IS E1 RC AT 52  
DEFAULT MLEVEL IS ATOM  
GGCAT IS LIN LOC SAT AT 28  
GGCAT IS LIN LOC SAT AT 33  
GGCAT IS LIN LOC SAT AT 37  
GGCAT IS LIN LOC SAT AT 50  
GGCAT IS LOC AT 52

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED  
NUMBER OF NODES IS 54

STEREO ATTRIBUTES: NONE

L28	22	SEA	FILE=REGISTRY	SUB=L24	SSS	FUL	L26
L31	1	SEA	FILE=REGISTRY	ABB=ON	PLU=ON	116644-53-2	
L35	21	SEA	FILE=REGISTRY	ABB=ON	PLU=ON	L28	NOT L31
L38	1	SEA	FILE=REGISTRY	ABB=ON	PLU=ON	116666-63-8	
L39	20	SEA	FILE=REGISTRY	ABB=ON	PLU=ON	L35	NOT L38
L40	13	SEA	FILE=HCAPLUS	ABB=ON	PLU=ON	L39	

=> d 140 ibib abs hitstr 1-13

L40 ANSWER 1 OF 13 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:531365 HCAPLUS

DOCUMENT NUMBER: 141:65063

TITLE: Use of a combination containing a non-nucleoside reverse transcriptase inhibitor (NNRTI) with an inhibitor of cytochrome p450 for the treatment of HIV-1 infection

INVENTOR(S): Cordingley, Michael Graham

PATENT ASSIGNEE(S): Boehringer Ingelheim International GmbH, Germany

SOURCE: PCT Int. Appl., 23 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004054586	A1	20040701	WO 2003-EP14224	20031215
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2510143	AA	20040701	CA 2003-2510143	20031215
AU 2003296647	A1	20040709	AU 2003-296647	20031215
US 2004152625	A1	20040805	US 2003-736301	20031215
EP 1575595	A1	20050921	EP 2003-813119	20031215
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003017095	A	20051025	BR 2003-17095	20031215
NO 2005003455	A	20050810	NO 2005-3455	20050715
PRIORITY APPLN. INFO.:			US 2002-433690P	P 20021216
			WO 2003-EP14224	W 20031215

AB An improved method for using a NNRTI in the treatment of HIV-1 infection comprises administering to a human in need of treatment for HIV-1 infection a therapeutically effective amount of the NNRTI, or a

pharmaceutically acceptable salt thereof, and an amount of an inhibitor of cytochrome P 450 that is sufficient to elevate, enhance, or extend plasma concns. of said NNRTI.

IT 710282-37-4

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

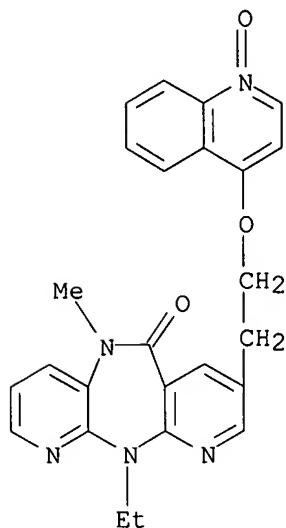
(non-nucleoside reverse transcriptase inhibitor combination with cytochrome P 450 inhibitor for treatment of HIV-1 infection)

RN 710282-37-4 HCAPLUS

CN Acetic acid, methoxy-, (1S,2S)-2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl ester, mixt. with 11-ethyl-5,11-dihydro-5-methyl-8-[2-[(1-oxido-4-quinolinyl)oxylethyl]-6H-dipyrido[3,2-b:2',3'-e][1,4]diazepin-6-one (9CI) (CA INDEX NAME)

CM 1

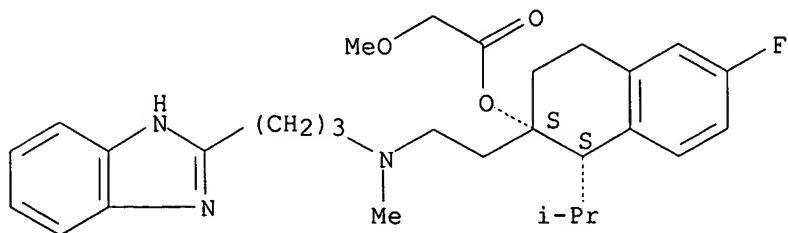
CRN 380378-81-4  
CMF C25 H23 N5 O3



CM 2

CRN 116644-53-2  
CMF C29 H38 F N3 O3

Absolute stereochemistry.



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 2 OF 13 HCAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 2000:405028 HCAPLUS  
 DOCUMENT NUMBER: 133:217516  
 TITLE: High affinity interaction of mibepradil with voltage-gated calcium and sodium channels  
 AUTHOR(S): Eller, Philipp; Berjukov, Stanislav; Wanner, Siegmund; Huber, Irene; Hering, Steffen; Knaus, Hans-Gunther; Toth, Geza; Kimball, S. David; Striessnig, Jorg  
 CORPORATE SOURCE: Institut fur Biochemische Pharmakologie, Innsbruck, A-6020, Austria  
 SOURCE: British Journal of Pharmacology (2000), 130(3), 669-677  
 CODEN: BJPCBM; ISSN: 0007-1188  
 PUBLISHER: Nature Publishing Group  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB Mibepradil is a novel Ca<sup>2+</sup> antagonist which blocks both high-voltage activated and low voltage-activated Ca<sup>2+</sup> channels. Although L-type Ca<sup>2+</sup> channel block was demonstrated in functional expts. its mol. interaction with the channel has not yet been studied. We therefore investigated the binding of [<sup>3</sup>H]-mibepradil and a series of mibepradil analogs to L-type Ca<sup>2+</sup> channels in different tissues. [<sup>3</sup>H]-Mibepradil labeled a single class of high affinity sites on skeletal muscle L-type Ca<sup>2+</sup> channels (KD of 2.5±0.4 nM, B<sub>max</sub> = 56.4±2.3 pmol mg<sup>-1</sup> of protein). Mibepradil (and a series of analogs) partially inhibited (+)-[<sup>3</sup>H]-isradipine binding to skeletal muscle membranes but stimulated binding to brain L-type Ca<sup>2+</sup> channels and α<sub>1C</sub>-subunits expressed in tsA201 cells indicating a tissue-specific, non-competitive interaction between the dihydropyridine and mibepradil binding domain. [<sup>3</sup>H]-Mibepradil also labeled a heterogeneous population of high affinity sites in rabbit brain which was inhibited by a series of nonspecific Ca<sup>2+</sup> and Na<sup>+</sup>-channel blockers. Mibepradil and its analog RO40-6040 had high affinity for neuronal voltage-gated Na<sup>+</sup>-channels as confirmed in binding (apparent K<sub>i</sub> values of 17 and 1.0 nM, resp.) and functional expts. (40% use-dependent inhibition of Na<sup>+</sup>-channel current by 1 μM mibepradil in GH3 cells). Our data demonstrate that mibepradil binds to voltage-gated L-type Ca<sup>2+</sup> channels with very high affinity and is also a potent blocker of voltage-gated neuronal Na<sup>+</sup>-channels. More lipophilic mibepradil analogs may possess neuroprotective properties like other nonselective Ca<sup>2+</sup>-/Na<sup>+</sup>-channel blockers.

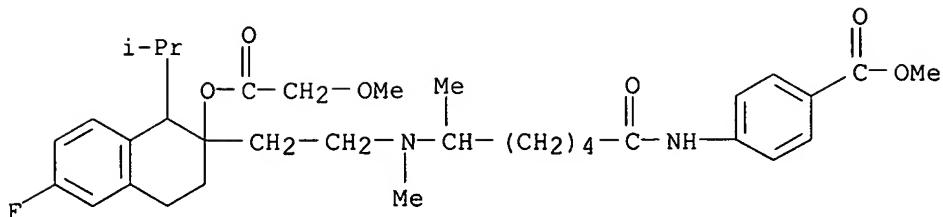
IT 291307-58-9, Ro 19-8287

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(high affinity interaction of mibepradil with voltage-gated calcium and sodium channels)

RN 291307-58-9 HCAPLUS

CN Benzoic acid, 4-[[6-[[2-[[6-fluoro-1,2,3,4-tetrahydro-2-[(methoxycetyl)oxy]-1-(1-methylethyl)-2-naphthalenyl]ethyl]methylamino]-1-oxoheptyl]amino]-, methyl ester (9CI) (CA INDEX NAME)



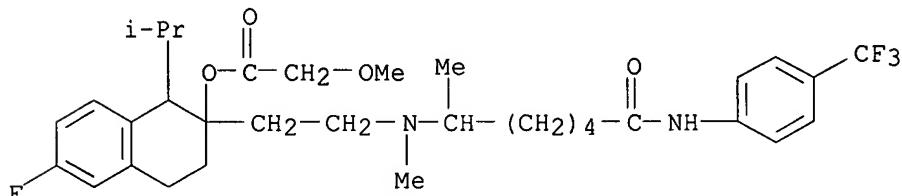
IT 291307-57-8, Ro 19-6945

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(high affinity interaction of mibebradil with voltage-gated calcium and sodium channels)

RN 291307-57-8 HCAPLUS

CN Acetic acid, methoxy-, 6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-[2-[methyl[1-methyl-6-oxo-6-[[4-(trifluoromethyl)phenyl]amino]hexyl]amino]ethyl]-2-naphthalenyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 3 OF 13 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:819361 HCAPLUS

DOCUMENT NUMBER: 132:44979

TITLE: Nitrate salts of antihypertensive medicines

INVENTOR(S): Del, Soldato Piero

PATENT ASSIGNEE(S): Nicox S. A., Fr.

SOURCE: PCT Int. Appl., 77 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9967231	A1	19991229	WO 1999-EP4138	19990615
W: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GE, HR, HU, IL, IN, IS, JP, KP, KR, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
IT 1301759	B1	20000707	IT 1998-MI1408	19980619
CA 2335356	AA	19991229	CA 1999-2335356	19990615

AU 9945139	A1	20000110	AU 1999-45139	19990615
AU 770387	B2	20040219		
EP 1087953	A1	20010404	EP 1999-927990	19990615
EP 1087953	B1	20041117		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE, SI, LT, FI, RO				
BR 9911305	A	20011023	BR 1999-11305	19990615
JP 2002518492	T2	20020625	JP 2000-555885	19990615
RU 2235097	C2	20040827	RU 2000-131690	19990615
AT 282600	E	20041215	AT 1999-927990	19990615
ES 2234265	T3	20050616	ES 1999-927990	19990615
ZA 2000006136	A	20020130	ZA 2000-6136	20001030
US 6645965	B1	20031111	US 2000-719164	20001212
US 2004147575	A1	20040729	US 2003-671746	20030929
PRIORITY APPLN. INFO.:				
			IT 1998-MI1408	A 19980619
			WO 1999-EP4138	W 19990615
			US 2000-719164	A3 20001212

OTHER SOURCE(S): MARPAT 132:44979

AB Nitric acid salts of drugs have antihypertensive activity. Some example salts prepared and showing antihypertensive activity were: timolol, propranolol, sildenafil, valsartan, hydralazine, nicardipine, verapamil, and amiloride nitrate salts.

IT 252951-80-7

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(nitrate salts of antihypertensive medicines)

RN 252951-80-7 HCPLUS

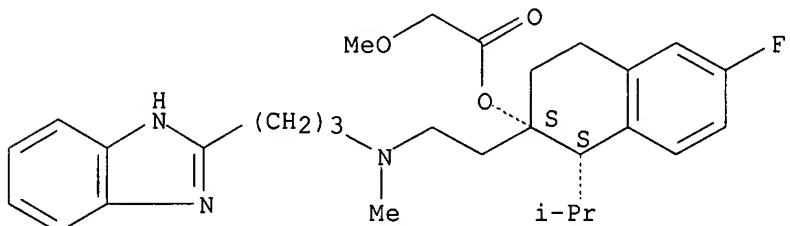
CN Acetic acid, methoxy-, (1S,2S)-2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl ester, nitrate (9CI) (CA INDEX NAME)

CM 1

CRN 116644-53-2

CMF C29 H38 F N3 O3

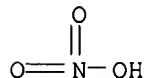
Absolute stereochemistry.



CM 2

CRN 7697-37-2

CMF H N O3

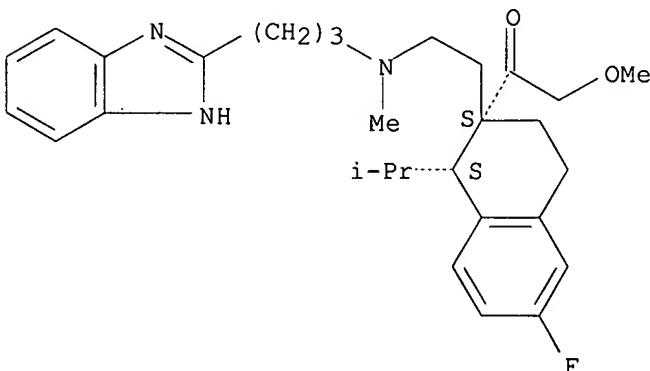


REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 4 OF 13 HCAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 1999:104627 HCAPLUS  
 DOCUMENT NUMBER: 130:205140  
 TITLE: Potential-dependent, T-type calcium channel inhibitors for treatment or prevention of pollakiuria or urinary incontinence  
 INVENTOR(S): Narita, Kazuhisa; Koga, Ichiro; Okada, Atsushi  
 PATENT ASSIGNEE(S): Nippon Kayaku Co., Ltd., Japan  
 SOURCE: Jpn. Kokai Tokkyo Koho, 4 pp.  
 CODEN: JKXXAF  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Japanese  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 11035483	A2	19990209	JP 1998-128463	19980512
PRIORITY APPLN. INFO.:			JP 1997-144503	A 19970520
AB	Potential-dependent, T-type calcium channel inhibitors e.g. [1S, 2S]-2-[2-[[3-[2-benzimidazolyl]propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-isopropyl-2-naphthylmethoxyacetate and 7-[4-[4,4'-difluorobenzohydryl]piperadino-1-methyl]-2-[[2-hydroxyethyl]amino]-4-isopropyl-2,4,6-cycloheptatrien-1-one for treatment or prevention of pollakiuria or urinary incontinence are claimed.			
IT	220873-01-8			
	RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)			
	(potential-dependent, T-type calcium channel inhibitors for treatment or prevention of pollakiuria or urinary incontinence)			
RN	220873-01-8	HCAPLUS		
CN	Ethanone, 1-[(1S,2S)-2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl]-2-methoxy- (9CI) (CA INDEX NAME)			

Absolute stereochemistry.

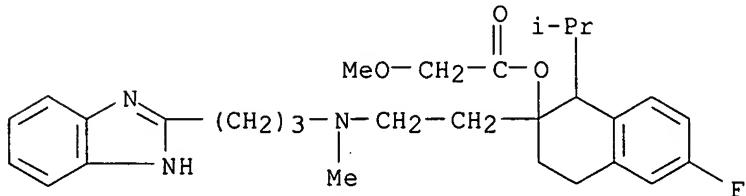


L40 ANSWER 5 OF 13 HCAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 1998:721683 HCAPLUS

DOCUMENT NUMBER: 129:330729  
 TITLE: Preparation of mibefradil I.  
 INVENTOR(S): Fleming, Michael Paul; Harrington, Peter John  
 PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.  
 SOURCE: PCT Int. Appl., 21 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

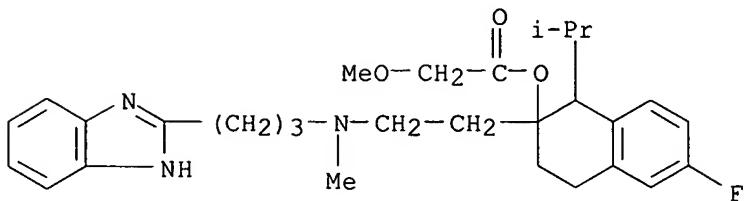
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9849149	A1	19981105	WO 1998-EP2416	19980423
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9876477	A1	19981124	AU 1998-76477	19980423
PRIORITY APPLN. INFO.:			US 1997-45151P	P 19970430
			WO 1998-EP2416	W 19980423

OTHER SOURCE(S): CASREACT 129:330729  
 AB 2-[2-[(3-(1H-benzimidazol-2-yl)propyl)methylamino]ethyl]-6-fluoro-1-isopropyl-1,2,3,4-tetrahydronaphthalen-2-yl methoxyacetate was prepared by reducing N-[3-(1H-benzimidazol-2-yl)propyl]-2-(6-fluoro-2-hydroxy-1-isopropyl-1,2,3,4-tetrahydronaphthalen-2-yl)-N-methylacetamide to give 2-[2-[(3-(1H-benzimidazol-2-yl)propyl)methylamino]ethyl]-6-fluoro-1-isopropyl-1,2,3,4-tetrahydronaphthalen-2-ol and contacting the latter with MeOCH<sub>2</sub>CO<sub>2</sub>H or an activated derivative thereof.  
 IT 213272-70-9P, 2-[2-[(3-(1H-Benzimidazol-2-yl)propyl)methylamino]ethyl]-6-fluoro-1-isopropyl-1,2,3,4-tetrahydronaphthalen-2-yl methoxyacetate 213272-71-0P, 2-[2-[(3-(1H-Benzimidazol-2-yl)propyl)methylamino]ethyl]-6-fluoro-1-isopropyl-1,2,3,4-tetrahydronaphthalen-2-yl methoxyacetate dihydrochloride  
 RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)  
 (preparation of mibefradil)  
 RN 213272-70-9 HCPLUS  
 CN Acetic acid, methoxy-, 2-[2-[(3-(1H-benzimidazol-2-yl)propyl)methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl ester (9CI) (CA INDEX NAME)



RN 213272-71-0 HCPLUS  
 CN Acetic acid, methoxy-, 2-[2-[(3-(1H-benzimidazol-2-yl)propyl)methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-

2-naphthalenyl ester, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 6 OF 13 HCAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 1998:721682 HCAPLUS  
 DOCUMENT NUMBER: 129:343493  
 TITLE: Preparation of mibefradil II.  
 INVENTOR(S): Harrington, Peter John; Wong, Jim-wah  
 PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.  
 SOURCE: PCT Int. Appl., 22 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9849148	A1	19981105	WO 1998-EP2415	19980423
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9879092	A1	19981124	AU 1998-79092	19980423
PRIORITY APPLN. INFO.:			US 1997-46795P	P 19970430
			WO 1998-EP2415	W 19980423

OTHER SOURCE(S): CASREACT 129:343493

AB A process for preparation of 2-[2-[(3-(1H-benzimidazol-2-yl)propyl)methylamino]ethyl]-6-fluoro-1-isopropyl-1,2,3,4-tetrahydronaphthalen-2-yl methoxyacetate via contacting (6-fluoro-2-hydroxy-1-isopropyl-1,2,3,4-tetrahydronaphthalen-2-yl)acetic acid or an activated derivative thereof with [3-(1H-benzimidazol-2-yl)propyl)methylamine to form N-[3-(1H-benzimidazol-2-yl)propyl]-2-(6-fluoro-2-hydroxy-1-isopropyl-1,2,3,4-tetrahydronaphthalen-2-yl)-N-methylacetamide is claimed.

IT 213272-70-9P, 2-[2-[(3-(1H-Benzimidazol-2-yl) propyl)methylamino]ethyl]-6-fluoro-1-isopropyl-1,2,3,4-tetrahydronaphthalen-2-yl methoxyacetate

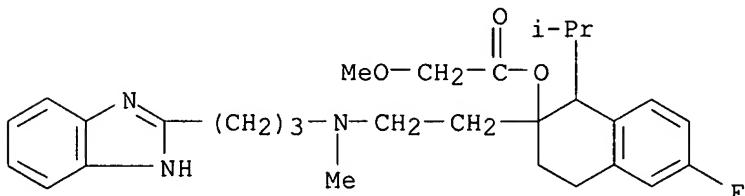
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP

## (Preparation)

(preparation of mibefradil)

RN 213272-70-9 HCAPLUS

CN Acetic acid, methoxy-, 2-[2-[(3-(1H-benzimidazol-2-yl)propyl)methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 7 OF 13 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:721681 HCAPLUS

DOCUMENT NUMBER: 129:343492

TITLE: Preparation of mibefradil III.

INVENTOR(S): Harrington, Peter John; Wong, Jim-wah

PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.

SOURCE: PCT Int. Appl., 19 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9849147	A1	19981105	WO 1998-EP2406	19980423
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9876473	A1	19981124	AU 1998-76473	19980423
PRIORITY APPLN. INFO.:			US 1997-45150P	P 19970430
			WO 1998-EP2406	W 19980423

OTHER SOURCE(S): CASREACT 129:343492

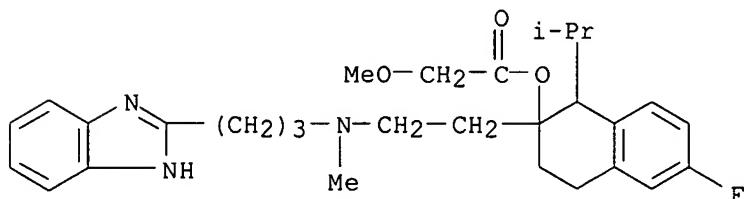
AB 2-[2-[(3-(1H-benzimidazol-2-yl)propyl)methylamino]ethyl]-6-fluoro-1-isopropyl-1,2,3,4-tetrahydronaphthalen-2-yl methoxyacetate was prepared by contacting [3-(1H-benzimidazol-2-yl)propyl)methylamine with (6-fluoro-2-hydroxy-1-isopropyl-1,2,3,4-tetrahydronaphthalen-2-yl)acetonitrile in the presence of H2 and a hydrogenation catalyst, followed by contacting the resulting 2-[2-[(3-(1H-benzimidazol-2-yl)propyl)methylamino]ethyl]-6-fluoro-1-isopropyl-1,2,3,4-tetrahydronaphthalen-2-ol with MeOCH2CO2H or an activated derivative thereof.

IT 213272-70-9P, 2-[2-[(3-(1H-benzimidazol-2-yl)propyl)methylamino]ethyl]-6-fluoro-1-isopropyl-1,2,3,4-tetrahydronaphthalen-2-yl methoxyacetate

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)  
 (preparation of mibefradil)

RN 213272-70-9 HCAPLUS

CN Acetic acid, methoxy-, 2-[2-[(3-(1H-benzimidazol-2-yl)propyl)methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 8 OF 13 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:618399 HCAPLUS

DOCUMENT NUMBER: 129:245150

TITLE: Improved preparation of mibefradil via an acetonitrile anion

INVENTOR(S): Wong, Jim-wah; Harrington, Peter J.

PATENT ASSIGNEE(S): Roche Colorado Corp., USA

SOURCE: U.S., 6 pp.

CODEN: USXXAM

DOCUMENT TYPE: Patent

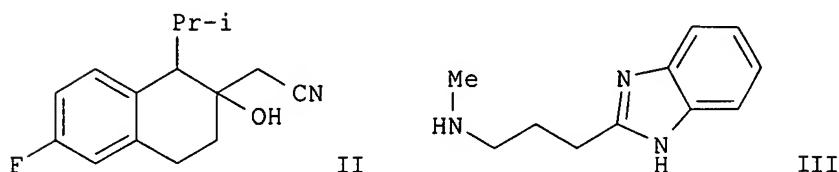
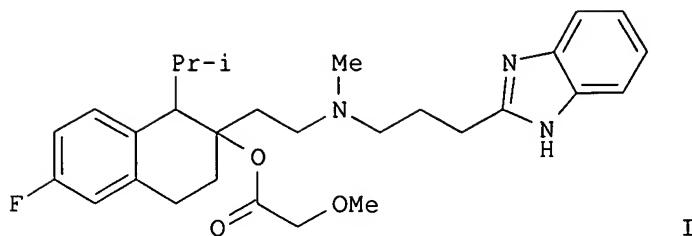
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5811557	A	19980922	US 1998-60401	19980414
PRIORITY APPLN. INFO.:			US 1998-60401	19980414
OTHER SOURCE(S):	CASREACT	129:245150		

GI

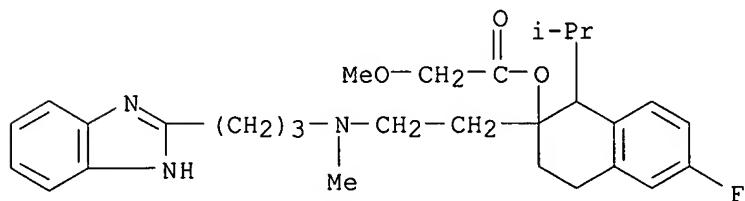


AB A method of preparing 2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1-isopropyl-1,2,3,4-tetrahydronaphthalen-2-yl methoxyacetate (I) comprises contacting 6-fluoro-1-isopropyl-3,4-dihydro-1H-naphthalen-2-one with the anion of acetonitrile in an aprotic polar solvent, contacting the thus-formed (6-fluoro-2-hydroxy-1-isopropyl-1,2,3,4-tetrahydronaphthalen-2-yl)acetonitrile (II) with [3-(1H-benzimidazol-2-yl)propyl]methylamine (III) in the presence of hydrogen and a hydrogenation catalyst, and finally esterifying the obtained 2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1-isopropyl-1,2,3,4-tetrahydronaphthalen-2-ol with methoxyacetic acid or an activated derivative of it. The invention is particularly applicable to the preparation of the antihypertensive mibepradil, namely (1S,2S)-I, and its di-HCl salt. The intermediate nitrile II is a new compound

IT 213272-70-9P, 2-[2-[[3-(1H-Benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1-isopropyl-1,2,3,4-tetrahydronaphthalen-2-yl methoxyacetate  
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)  
(improved preparation of mibepradil via an acetonitrile anion)

RN 213272-70-9 HCAPLUS

CN Acetic acid, methoxy-, 2-[2-[(3-(1H-benzimidazol-2-yl)propyl)methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl ester (9CI) (CA INDEX NAME)

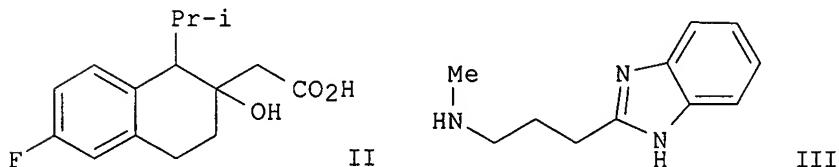
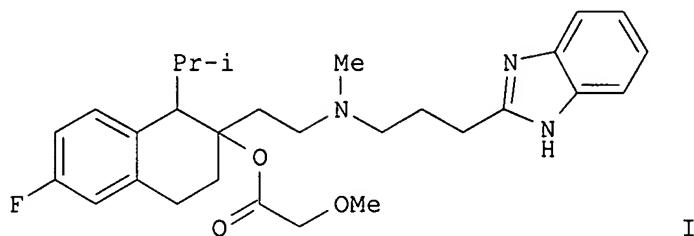


REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 9 OF 13 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:618398 HCAPLUS  
DOCUMENT NUMBER: 129:245149  
TITLE: Improved preparation of mibefradil via a  
naphthalenylacetic acid  
INVENTOR(S): Harrington, Peter J.; Wong, Jim-wah  
PATENT ASSIGNEE(S): Roche Colorado Corp., USA  
SOURCE: U.S., 7 pp.  
CODEN: USXXAM  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5811556	A	19980922	US 1998-60168	19980414
PRIORITY APPLN. INFO.:			US 1998-60168	19980414
OTHER SOURCE(S):	CASREACT	129:245149		
GI				



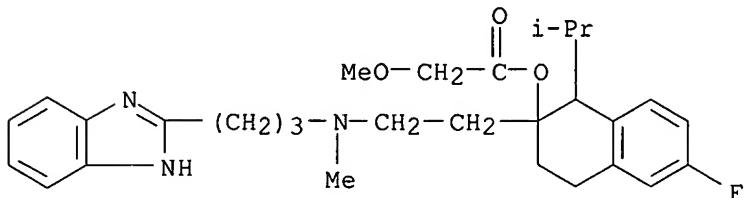
AB A method of preparing 2-[2-[(3-(1H-benzimidazol-2-yl)propyl)methylamino]ethyl]-6-fluoro-1-isopropyl-1,2,3,4-tetrahydronaphthalen-2-yl methoxyacetate (I) comprises contacting (6-fluoro-2-hydroxy-1-isopropyl-1,2,3,4-tetrahydronaphthalen-2-yl)acetic acid (II) or an activated derivative with [3-(1H-benzimidazol-2-yl)propyl)methylamine(III), reducing the formed amide function to a tertiary amine, and esterifying the obtained hydroxy amine with methoxyacetic acid or an activated derivative of it. The invention is particularly applicable to the preparation of the antihypertensive mibepradil, i.e., (1S,2S)-I, and its di-HCl salt. The intermediate amide, namely N-[3-(1H-benzimidazol-2-yl)propyl]-2-(6-fluoro-2-hydroxy-1-isopropyl-1,2,3,4-tetrahydronaphthalen-2-yl)-N-methylacetamide, is a new compound 213272-70-9P, 2-[2-[(3-(1H-Benzimidazol-2-yl)propyl)methylamino]ethyl]-6-fluoro-1-isopropyl-1,2,3,4-tetrahydronaphthalen-2-yl methoxyacetate 213272-71-0P, 2-[2-[(3-(1H-Benzimidazol-2-yl)propyl)methylamino]ethyl]-6-fluoro-1-isopropyl-1,2,3,4-tetrahydronaphthalen-2-yl methoxyacetate dihydrochloride  
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP

## (Preparation)

(preparation of mibefradil via a naphthalenylacetic acid)

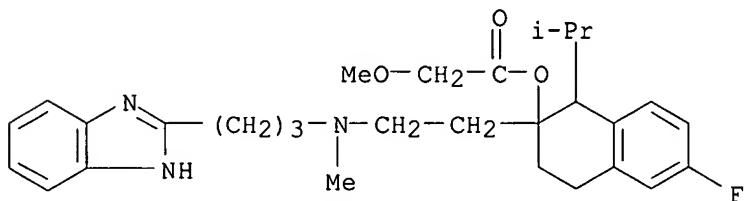
RN 213272-70-9 HCPLUS

CN Acetic acid, methoxy-, 2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl ester (9CI) (CA INDEX NAME)



RN 213272-71-0 HCPLUS

CN Acetic acid, methoxy-, 2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl ester, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 10 OF 13 HCPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1997:424055 HCPLUS

DOCUMENT NUMBER: 127:144696

TITLE: Metabolism of the calcium antagonist, mibefradil (POSICOR, Ro 40-5967). Part III. Comparative pharmacokinetics of mibefradil and its major metabolites in rat, marmoset, cynomolgus monkey and man

AUTHOR(S): Wiltshire, H. R.; Sutton, B. M.; Heeps, G.; Betty, A. M.; Angus, D. W.; Harris, S. R.; Worth, E.; Welker, H. A.

CORPORATE SOURCE: Department of Pharmacokinetics and Metabolism, Roche Products Ltd, Welwyn Garden City, AL7 3AY, UK

SOURCE: Xenobiotica (1997), 27(6), 557-571  
CODEN: XENOHB; ISSN: 0049-8254

PUBLISHER: Taylor &amp; Francis

DOCUMENT TYPE: Journal

LANGUAGE: English

AB 1. The metabolism of mibefradil has been examined in rat, marmoset, cynomolgus monkey and man after single and multiple oral administration. 2.

Metabolites typically represent between 50 and 80% of the circulating drug-related material after single oral doses of mibepradil to man, rat and marmoset. They arise by a combination of enzymic processes: cytochrome P 450-mediated oxidation at saturated and unsatd. carbon atoms, cytochrome P 450-catalyzed dealkylation and hydrolysis of the ester side-chain. 3. Plasma levels of mibepradil in the cynomolgus monkey are extremely low as a result of very efficient first-pass hydrolysis of its side-chain to give the corresponding alc. Steady-state concns. of this metabolite are comparable with those of the parent drug in man and marmoset, but are relatively low in rat plasma. 4. Hydroxylation at the benzylic carbon of the tetrahydronaphthyl ring leads to further important metabolites in primates, whereas the products of O- and N-demethylation are found in small amts. in all four species. 5. Ests. of the exposure of the various species to the principal metabolites indicate that the choice of the rat, marmoset and cynomolgus monkey for the toxicol. assessment of mibepradil was appropriate.

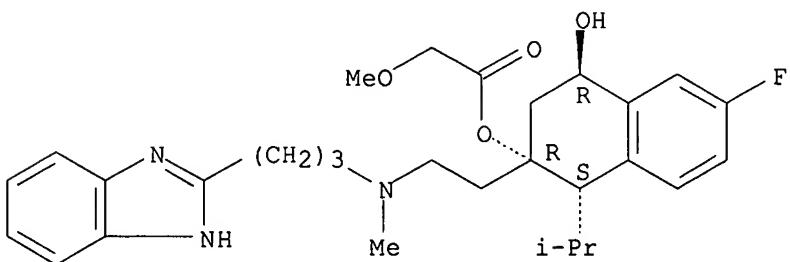
IT 193351-45-0

RL: BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)  
(metabolism of the calcium antagonist mibepradil in humans and lab animals)

RN 193351-45-0 HCAPLUS

CN Acetic acid, methoxy-, 2-[2-[(3-(1H-benzimidazol-2-yl)propyl)methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-4-hydroxy-1-(1-methylethyl)-2-naphthalenyl ester, [1S-(1 $\alpha$ ,2 $\alpha$ ,4 $\beta$ )]- (9CI)  
(CA INDEX NAME)

Absolute stereochemistry.



L40 ANSWER 11 OF 13 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1997:424054 HCAPLUS

DOCUMENT NUMBER: 127:144695

TITLE: Metabolism of the calcium antagonist, mibepradil (POSICOR, Ro 40-5967). Part II. Metabolism in hepatic microsomes from rat, marmoset, cynomolgus monkey, rabbit and man

AUTHOR(S): Wiltshire, H. R.; Sutton, B. M.; Heeps, G.; Betty, A. M.; Angus, D. W.; Madigan, M. J.; Sharp, S. R.

CORPORATE SOURCE: Pharmacokinetics and Metabolism Department, Roche Products Ltd, Welwyn Garden City, AL7 3AY, UK

SOURCE: Xenobiotica (1997), 27(6), 539-556

CODEN: XENOHB; ISSN: 0049-8254

PUBLISHER: Taylor & Francis

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The calcium antagonist, mibepradil, is converted to some 30 metabolites after incubation with hepatic microsomes from the rat, marmoset, cynomolgus monkey, rabbit and man. The wide inter-species differences in

the

metabolic profile stem mainly from variations in the activity of the microsomal esterase, which hydrolyses the ester side-chain of mibepradil to give the alc. metabolite, Ro 40-5966. Hydrolysis is especially marked in

cynomolgus monkey and rabbit, less in man and least in the rat and marmoset. The biotransformation of this alc. metabolite by cytochromes P 450 is more facile than that of the parent compound, leads to fewer metabolites and the metabolic profiles in all species are similar. The most important cytochrome P 450-mediated metabolic process in microsomes in all species is hydroxylation at the benzylic carbon atom of the tetrahydronaphthyl group; further oxidation of the resultant secondary alc. to a ketone also occurs. These reactions indicate the route of the biosynthetic pathway which leads to the major, naphthyl-glucuronide metabolites previously isolated from rat bile. Dealkylation of the tertiary amino group is also important and leads to compds. lacking either the N-Me group or the propylbenzimidazole moiety. Hydroxylation of the benzimidazole ring at both the 4- and 5-positions is largely restricted to mibepradil and does not occur to a significant extent with Ro 40-5966.

IT 144917-60-2 193351-45-0 193464-93-6

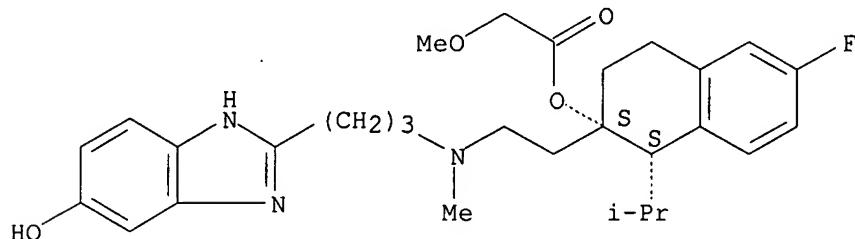
193464-95-8

RL: BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)  
(metabolism of the calcium antagonist mibepradil in humans and lab animals)

RN 144917-60-2 HCPLUS

CN Acetic acid, methoxy-, 6-fluoro-1,2,3,4-tetrahydro-2-[2-[[3-(5-hydroxy-1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-1-(1-methylethyl)-2-naphthalenyl ester, (1S-cis)- (9CI) (CA INDEX NAME)

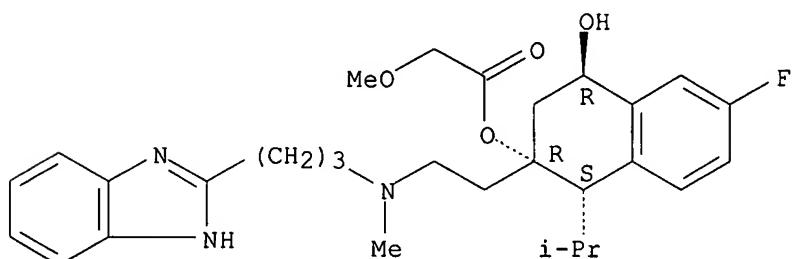
Absolute stereochemistry.



RN 193351-45-0 HCPLUS

CN Acetic acid, methoxy-, 2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-4-hydroxy-1-(1-methylethyl)-2-naphthalenyl ester, [1S-(1α,2α,4β)]- (9CI)  
(CA INDEX NAME)

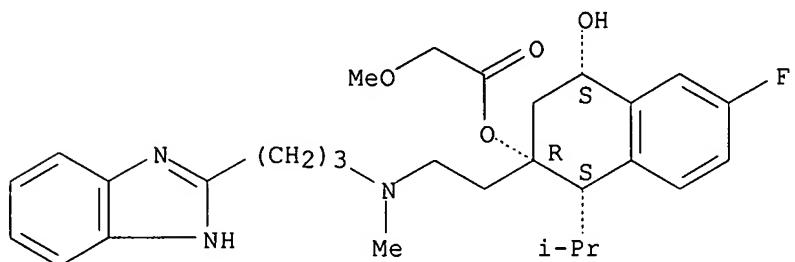
Absolute stereochemistry.



RN 193464-93-6 HCPLUS

CN Acetic acid, methoxy-, 2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-4-hydroxy-1-(1-methylethyl)-2-naphthalenyl ester, [1S-(1 $\alpha$ ,2 $\alpha$ ,4 $\alpha$ )]- (9CI) (CA INDEX NAME)

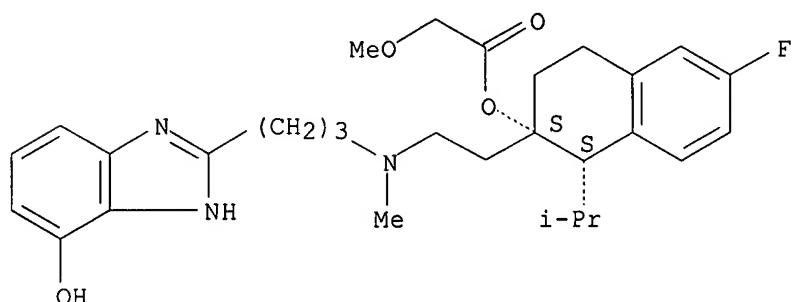
Absolute stereochemistry.



RN 193464-95-8 HCPLUS

CN Acetic acid, methoxy-, 6-fluoro-1,2,3,4-tetrahydro-2-[2-[[3-(4-hydroxy-1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-1-(1-methylethyl)-2-naphthalenyl ester, (1S-cis)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L40 ANSWER 12 OF 13 HCPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1993:15784 HCPLUS

DOCUMENT NUMBER: 118:15784

TITLE: Metabolism of calcium antagonist Ro 40-5967: a case history of the use of diode-array UV spectroscopy and thermospray-mass spectrometry in the elucidation of a complex metabolic pathway

AUTHOR(S): Wiltshire, H. R.; Harris, S. R.; Prior, K. J.; Kozlowski, U. M.; Worth, E.

CORPORATE SOURCE: Dep. Pharmacokinet. Metab., Roche Prod. Ltd., Welwyn Garden City/Herts., AL7 3AY, UK

SOURCE: Xenobiotica (1992), 22(7), 837-57  
CODEN: XENOHB; ISSN: 0049-8254

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The calcium antagonist, Ro 40-5967, is metabolized to a multitude of products by the rat and drug-related material is excreted predominantly via the bile. Diode-array, UV spectroscopy, following reverse phase HPLC separation of the partially purified metabolites, has been used to classify

these compds. into six spectral classes which have been correlated with different metabolic reactions. Connection of a mass spectrometer directly to the HPLC equipment by a thermospray interface, produced useful mass spectra. These, together with the UV spectra, enabled the structures of many metabolites to be elucidated. Confirmation of structural assignments was provided by NMR spectra of the major metabolites. Major metabolite pathways included N-demethylation (16% of the biliary metabolites), hydrolysis of the ester side-chain (32%), hydroxylation at 4- (19%) and 5- (29%) positions of the benzimidazole ring, aromatization of the tetrahydronaphthyl system (26%), loss of the benzimidazole (15%) and glucuronidation of hydroxyl groups (81%).

IT 144917-55-5 144917-60-2 144917-61-3

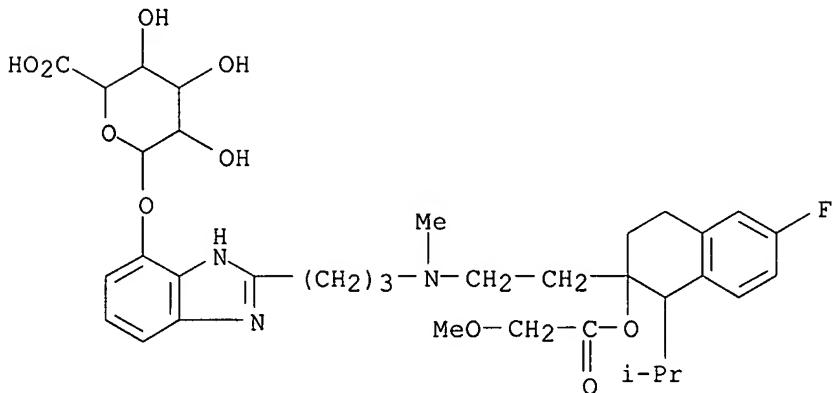
144917-69-1

RL: PROC (Process)

(as Ro 5967 metabolite, characterization of, by diode-array UV spectroscopy and thermospray-mass spectrometry)

RN 144917-55-5 HCPLUS

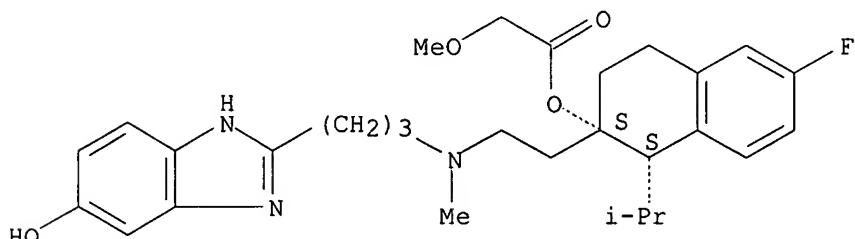
CN  $\beta$ -D-Glucopyranosiduronic acid, 2-[3-[[2-[6-fluoro-1,2,3,4-tetrahydro-2-[(methoxyacetyl)oxy]-1-(1-methylethyl)-2-naphthalenyl]ethyl]methylamino]propyl]-1H-benzimidazol-4-yl, (1S-cis)- (9CI) (CA INDEX NAME)



RN 144917-60-2 HCPLUS

CN Acetic acid, methoxy-, 6-fluoro-1,2,3,4-tetrahydro-2-[2-[[3-(5-hydroxy-1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-1-(1-methylethyl)-2-naphthalenyl ester, (1S-cis)- (9CI) (CA INDEX NAME)

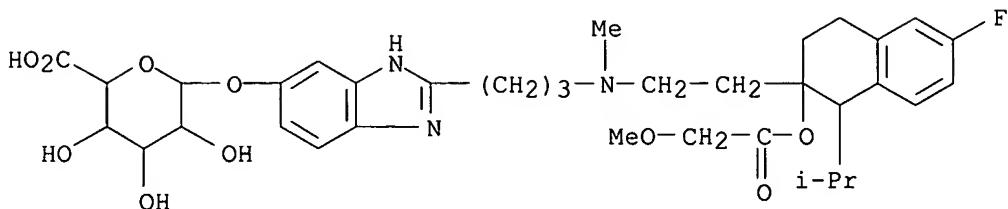
Absolute stereochemistry.



RN 144917-61-3 HCPLUS

CN  $\beta$ -D-Glucopyranosiduronic acid, 2-[3-[[2-[6-fluoro-1,2,3,4-tetrahydro-2-[(methoxyacetyl)oxy]-1-(1-methylethyl)-2-naphthalenyl]ethyl]methylamino]

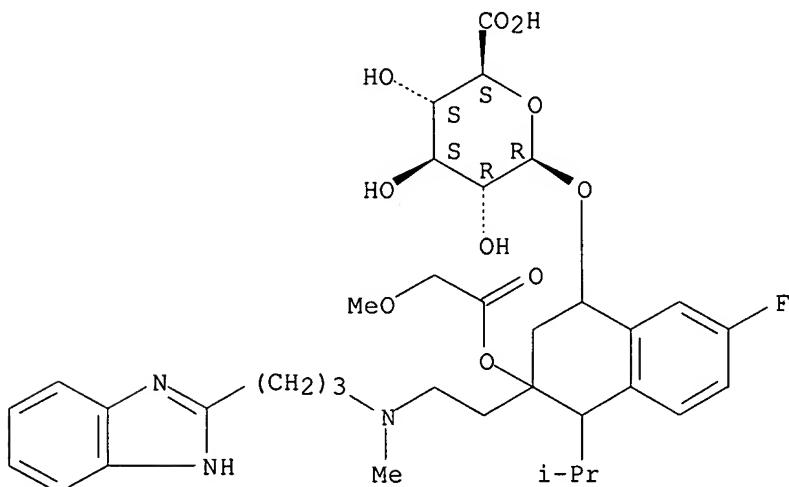
propyl]-1H-benzimidazol-5-yl, (1S-cis)- (9CI) (CA INDEX NAME)



RN 144917-69-1 HCPLUS

CN  $\beta$ -D-Glucopyranosiduronic acid, 3-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-7-fluoro-1,2,3,4-tetrahydro-3-[(methoxyacetyl)oxy]-4-(1-methylethyl)-1-naphthalenyl (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L40 ANSWER 13 OF 13 HCPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1988:549535 HCPLUS

DOCUMENT NUMBER: 109:149535

TITLE: Preparation of [(heterocyclalkylamino)ethyl]tetrahydronaphthalenes as cardiovascular agents

INVENTOR(S): Branca, Quirico; Jaunin, Roland; Maerki, Hans Peter; Marti, Fraenzi; Ramuz, Henri

PATENT ASSIGNEE(S): Hoffmann-La Roche, F., und Co. A.-G., Switz.

SOURCE: Eur. Pat. Appl., 37 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

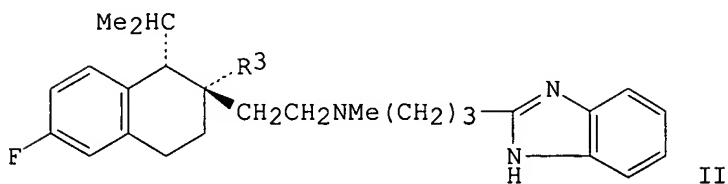
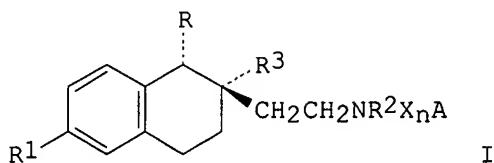
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
-----	-----	-----	-----	-----

EP 268148	A1	19880525	EP 1987-116251	19871104
EP 268148	B1	19911211		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
DK 8705599	A	19880515	DK 1987-5599	19871026
DK 171349	B1	19960916		
CA 1319144	A1	19930615	CA 1987-550190	19871026
CS 264350	B2	19890712	CS 1987-7874	19871103
AT 70267	E	19911215	AT 1987-116251	19871104
ES 2040234	T3	19931016	ES 1987-116251	19871104
ZA 8708362	A	19880727	ZA 1987-8362	19871106
AU 8780909	A1	19880519	AU 1987-80909	19871109
AU 600769	B2	19900823		
IL 84407	A1	19910916	IL 1987-84407	19871109
JP 63139171	A2	19880610	JP 1987-282287	19871110
JP 2504490	B2	19960605		
US 4808605	A	19890228	US 1987-119114	19871110
HU 60251	A2	19920828	HU 1987-5011	19871111
HU 215915	B	19990329		
FI 8705024	A	19880515	FI 1987-5024	19871113
FI 94414	B	19950531		
FI 94414	C	19950911		
NO 8704757	A	19880516	NO 1987-4757	19871113
NO 172237	B	19930315		
NO 172237	C	19930623		
CN 87107875	A	19880525	CN 1987-107875	19871113
CN 1028991	B	19950621		

PRIORITY APPLN. INFO.:

OTHER SOURCE(S):  
GI

MARPAT 109:149535

CH 1986-4565 A 19861114  
EP 1987-116251 A 19871104

AB The title compds. [I; A = substituted 2-(imidazol-2-yl)ethyl, (un)substituted benzimidazolyl, benzothiazolyl, etc.; R, R2 = alkyl; R1 = halo; R3 = OH, alkoxy, alkanoyloxy, alkoxyalkanoyloxy, etc.; X = C1-18 alkylene, optionally interrupted by 1,4-phenylene or -cyclohexylene; n = 0, 1] were prepared PhCH2O2CNMe(CH2)3CONHC6H4NH2-2 (preparation given) was refluxed 2 h in PhMe containing 4-MeC6H4SO3H and the product hydrogenized over Pd/C to give 2-[3-(methylamino)propyl]benzimidazole which was heated 30 min at 120° in (Me2CH)2NET with 2-(6-fluoro-1,2,3,4-tetrahydro-2-hydroxy-1α-isopropyl-2β-naphthyl)ethyl p-toluenesulfonate to give title compound II (R3 = OH). The latter was stirred overnight with MeOCH2COCl in CHCl3 containing (Me2CH)2NET to give II (R3 = MeOCH2CO2) (III)

which, at 0.3 mg/kg i.v., gave 25% and 86% increase in heart contractility and coronary blood flow, resp., in anesthetized dogs. Tablets were prepared each containing III 75, lactose 135, starch 70, Povidone K 30 15, talc 3, and Mg stearate 2 mg.

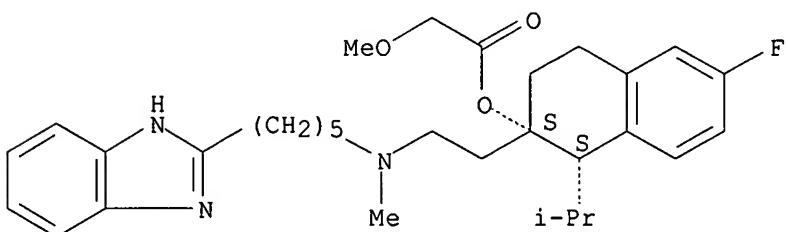
IT 116666-65-0P 116666-76-3P 116666-93-4P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (preparation of, as cardiovascular agent)

RN 116666-65-0 HCPLUS

CN Acetic acid, methoxy-, 2-[2-[[5-(1H-benzimidazol-2-yl)pentyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl ester, dihydrochloride, (1S-cis)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

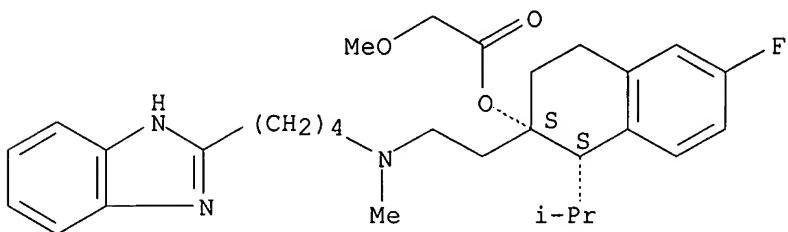


●2 HCl

RN 116666-76-3 HCPLUS

CN Acetic acid, methoxy-, 2-[2-[[4-(1H-benzimidazol-2-yl)butyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl ester, dihydrochloride, (1S-cis)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

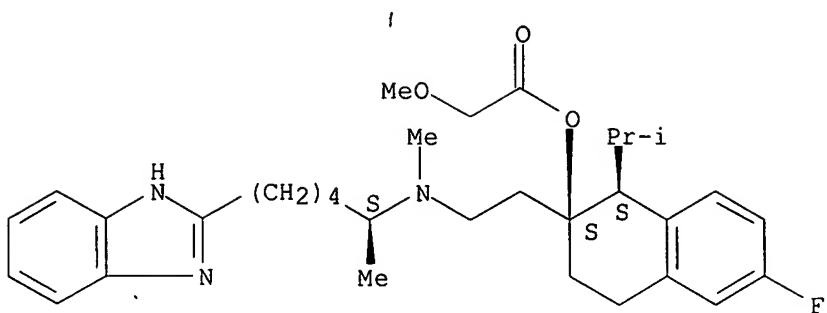


●2 HCl

RN 116666-93-4 HCPLUS

CN Acetic acid, methoxy-, 2-[2-[[5-(1H-benzimidazol-2-yl)-1-methylpentyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl ester, dihydrochloride, [1S-[1α,2α,2(R\*)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



●2 HCl

=> d que stat 141

L31 1 SEA FILE=REGISTRY ABB=ON PLU=ON 116644-53-2  
 L41 416 SEA FILE=HCAPLUS ABB=ON PLU=ON L31

=> d 141 ibib hitstr 1-5 400-416

L41 ANSWER 1 OF 416 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2006:107381 HCAPLUS

DOCUMENT NUMBER: 144:121407

TITLE: Relaxant responses to calcium channel antagonists and potassium channel opener in human saphenous vein

Ford, C.; Bieger, D.; Mong, K.; Tabrizchi, R.

AUTHOR(S): Division of Basic Medical Sciences, Faculty of  
 CORPORATE SOURCE: Medicine, Health Sciences Centre, Memorial University  
 of Newfoundland, St John's, NL, A1B 3V6, Can.

SOURCE: Autonomic & Autacoid Pharmacology (2006), 26(1), 7-13  
 CODEN: AAPUC3; ISSN: 1474-8665

PUBLISHER: Blackwell Publishing Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

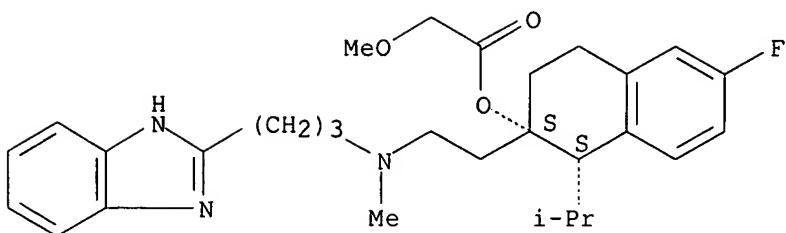
IT 116644-53-2, Mibepradil

RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (relaxant responses to calcium channel antagonists and potassium channel opener in human saphenous vein)

RN 116644-53-2 HCAPLUS

CN Acetic acid, methoxy-, (1S,2S)-2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



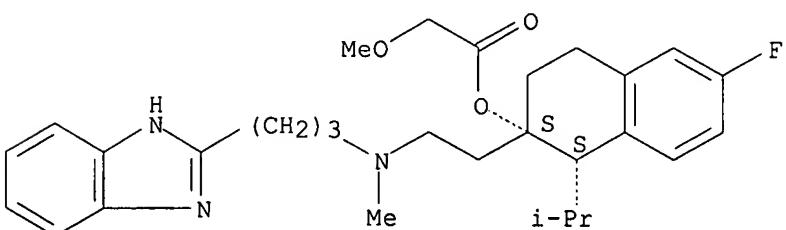
REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L41 ANSWER 2 OF 416 HCPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 2006:100738 HCPLUS  
 DOCUMENT NUMBER: 144:198849  
 TITLE: Novel dosage form comprising modified-release and immediate-release active ingredients  
 INVENTOR(S): Vaya, Navin; Karan, Rajesh Singh; Sadanand, Sunil; Gupta, Vinod Kumar  
 PATENT ASSIGNEE(S): India  
 SOURCE: U.S. Pat. Appl. Publ., 49 pp., Cont.-in-part of U.S. Ser. No. 630,446.  
 CODEN: USXXCO  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2006024365	A1	20060202	US 2005-134633	20050519
US 2004096499	A1	20040520	US 2003-630446	20030729
PRIORITY APPLN. INFO.:			IN 2002-MU697	A 20020805
			IN 2002-MU699	A 20020805
			IN 2003-MU80	A 20030122
			IN 2003-MU82	A 20030122
			US 2003-630446	A2 20030729

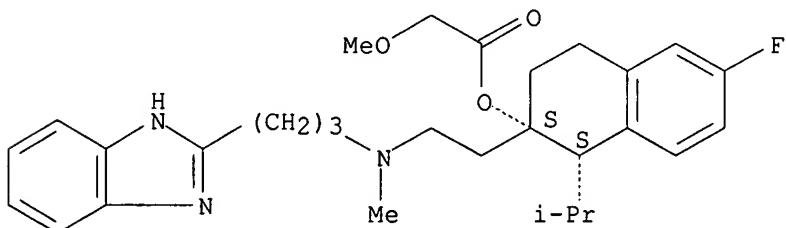
IT 116644-53-2, Mibefradil  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (novel dosage form comprising modified-release and immediate-release active ingredients)  
 RN 116644-53-2 HCPLUS  
 CN Acetic acid, methoxy-, (1S,2S)-2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L41 ANSWER 3 OF 416 HCAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 2006:56562 HCAPLUS  
 DOCUMENT NUMBER: 144:246907  
 TITLE: Inhibitory Effect of Efondipine on Aldosterone  
 Synthesis and Secretion in Human Adrenocarcinoma  
 (H295R) Cells  
 AUTHOR(S): Imagawa, Keiichi; Okayama, Satoshi; Takaoka, Minoru;  
 Kawata, Hiroyuki; Naya, Noriyuki; Nakajima, Tamio;  
 Horii, Manabu; Uemura, Shiro; Saito, Yoshihiko  
 CORPORATE SOURCE: First Department of Internal Medicine, Nara Medical  
 University, Kashihara, Nara, Japan  
 SOURCE: Journal of Cardiovascular Pharmacology (2006), 47(1),  
 133-138  
 CODEN: JCPCDT; ISSN: 0160-2446  
 PUBLISHER: Lippincott Williams & Wilkins  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 IT 116644-53-2, Mibepradil  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (inhibitory effect of efondipine on aldosterone synthesis and  
 secretion in human adrenocarcinoma cells)  
 RN 116644-53-2 HCAPLUS  
 CN Acetic acid, methoxy-, (1S,2S)-2-[2-[[3-(1H-benzimidazol-2-  
 yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-  
 2-naphthalenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L41 ANSWER 4 OF 416 HCAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 2006:51871 HCAPLUS  
 DOCUMENT NUMBER: 144:121827  
 TITLE: Methods for preventing pressure-induced apoptotic  
 neural-cell death in glaucoma patients by  
 administering inhibitors of TREK-1 and TRAAK potassium  
 channels  
 INVENTOR(S): Coroneo, Minas Theodore  
 PATENT ASSIGNEE(S): Davies Collison Cave, Australia  
 SOURCE: U.S. Pat. Appl. Publ., 13 pp., Cont.-in-part of U.S.  
 Ser. No. 84,604.  
 CODEN: USXXCO  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

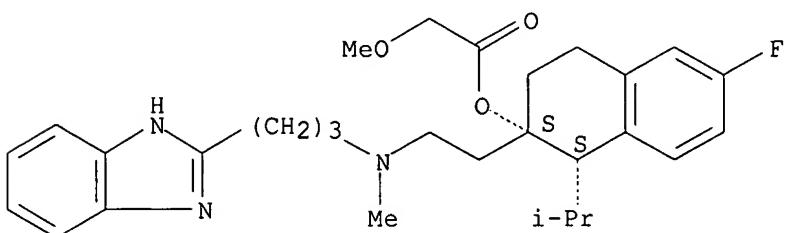
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2006013814	A1	20060119	US 2005-171531	20050630
US 2002187919	A1	20021212	US 2002-84604	20020227
PRIORITY APPLN. INFO.:			US 2000-649643	B1 20000829
			US 2002-84604	B2 20020227
			AU 2000-9267	A 20000808

IT 116644-53-2, Mibepradil  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
 (Biological study); USES (Uses)  
 (methods for preventing pressure-induced apoptotic neural-cell death in  
 glaucoma patients by administering inhibitors of TREK-1 and TRAAK  
 potassium channels)

RN 116644-53-2 HCPLUS

CN Acetic acid, methoxy-, (1S,2S)-2-[2-[[3-(1H-benzimidazol-2-  
 yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-  
 2-naphthalenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L41 ANSWER 5 OF 416 HCPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2006:5456 HCPLUS

DOCUMENT NUMBER: 144:205445

TITLE: Antihypertensive Effects of the Putative T-Type  
 Calcium Channel Antagonist Mibepradil Are Mediated by  
 the L-Type Calcium Channel Cav1.2

AUTHOR(S): Moosmang, Sven; Haider, Nicole; Bruederl, Birgit;  
 Welling, Andrea; Hofmann, Franz

CORPORATE SOURCE: Institut fuer Pharmakologie und Toxikologie,  
 Technische Universitaet Muenchen, Germany

SOURCE: Circulation Research (2006), 98(1), 105-110  
 CODEN: CIRUAL; ISSN: 0009-7330

PUBLISHER: Lippincott Williams & Wilkins

DOCUMENT TYPE: Journal

LANGUAGE: English

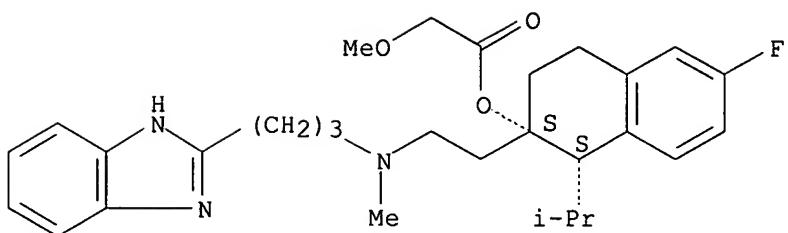
IT 116644-53-2, Mibepradil

RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU  
 (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (antihypertensive effects of the putative T-type calcium channel  
 antagonist mibepradil are mediated by the L-type calcium channel  
 Cav1.2)

RN 116644-53-2 HCPLUS

CN Acetic acid, methoxy-, (1S,2S)-2-[2-[[3-(1H-benzimidazol-2-  
 yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-  
 2-naphthalenyl ester (9CI) (CA INDEX NAME)

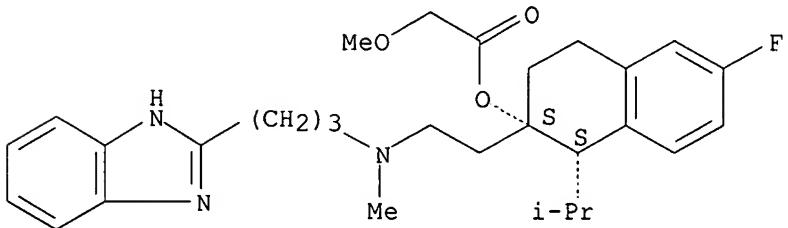
Absolute stereochemistry.



REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L41 ANSWER 400 OF 416 HCAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 1996:263166 HCAPLUS  
 DOCUMENT NUMBER: 124:332465  
 TITLE: Effect of mibefradil on left ventricular diastolic function in patients with congestive heart failure  
 Muntinga, H. J.; van der Vring, J. A. F. M.; Niemeyer, M. G.; van den Berg, F.; Knol, H. R.; Bernink, P. J. L. M.; van der Wall, E. E.; Blanksma, P. K.; Lie, K. I.  
 AUTHOR(S):  
 CORPORATE SOURCE: Dep. Cardiology, Martini Hospital, Groningen, 9700 RM, Neth.  
 SOURCE: Journal of Cardiovascular Pharmacology (1996), 27(5), 652-6  
 CODEN: JCPCDT; ISSN: 0160-2446  
 PUBLISHER: Lippincott-Raven  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 IT 116644-53-2, Mibefradil  
 RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (effect of mibefradil on left ventricular diastolic function in patients with congestive heart failure)  
 RN 116644-53-2 HCAPLUS  
 CN Acetic acid, methoxy-, (1S,2S)-2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L41 ANSWER 401 OF 416 HCAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 1996:205846 HCAPLUS  
 DOCUMENT NUMBER: 124:278618  
 TITLE: Antihypertensive properties of the novel calcium antagonist mibefradil (Ro 40-5967): A new generation

AUTHOR(S): of calcium antagonists?  
 Bernink, Peter J. L. M.; Prager, Gerold; Schelling, Arie; Kobrin, Isaac

CORPORATE SOURCE: Martini Ziekenhuis, Groningen, 9721 5W, Neth.

SOURCE: Hypertension (Dallas) (1996), 27(3, Pt. 1), 426-32

CODEN: HPRTDN; ISSN: 0194-911X

PUBLISHER: American Heart Association

DOCUMENT TYPE: Journal

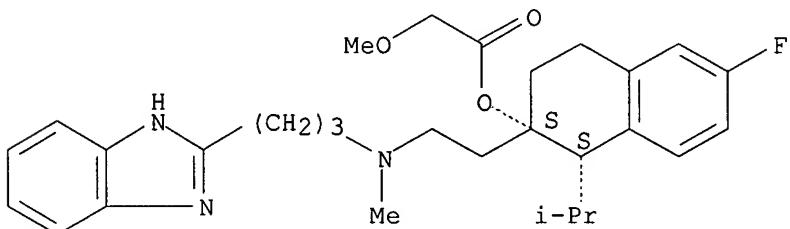
LANGUAGE: English

IT 116644-53-2, Mibefradil  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (antihypertensive properties of the novel calcium antagonist mibefradil (Ro 40-5967): a new generation of calcium antagonists)

RN 116644-53-2 HCPLUS

CN Acetic acid, methoxy-, (1S,2S)-2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L41 ANSWER 402 OF 416 HCPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 1996:138785 HCPLUS  
 DOCUMENT NUMBER: 124:250257  
 TITLE: Effects of a new calcium antagonist, mibefradil (Ro 40-5967), on silent ischemia in patients with stable chronic angina pectoris: A multicenter placebo-controlled study

AUTHOR(S): Braun, Shimon; Van Der Wall, Ernst E.; Emanuelsson, Haken; Kobrin, Isaac

CORPORATE SOURCE: Department Cardiology, Tel-Aviv Medical Center, Tel Aviv-Jaffa, 64239, Israel

SOURCE: Journal of the American College of Cardiology (1996), 27(2), 317-22

CODEN: JACCDI; ISSN: 0735-1097

PUBLISHER: Elsevier

DOCUMENT TYPE: Journal

LANGUAGE: English

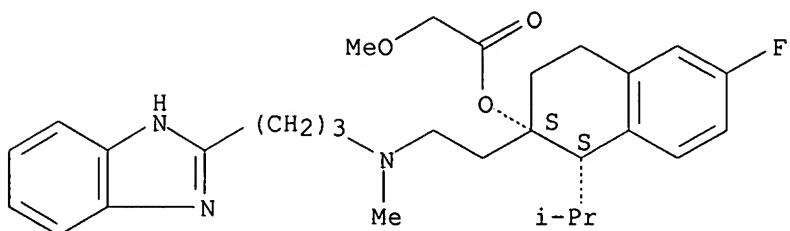
IT 116644-53-2, Mibefradil  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (effects of a new calcium antagonist, mibefradil (Ro 40-5967), on silent ischemia in human patients with stable chronic angina pectoris)

RN 116644-53-2 HCPLUS

CN Acetic acid, methoxy-, (1S,2S)-2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-

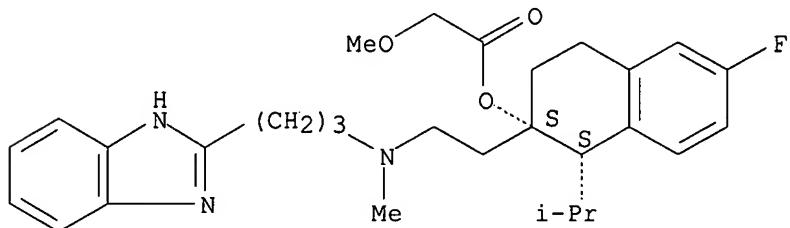
2-naphthalenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L41 ANSWER 403 OF 416 HCPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 1996:115986 HCPLUS  
 DOCUMENT NUMBER: 124:219315  
 TITLE: Hemodynamics, cardiac conduction and pharmacokinetics of mibefradil (Ro 40-5967), a novel calcium antagonist  
 Petrie, John R.; Glen, Stephen K.; MacMahon, Mark;  
 Crome, Renata; Meredith, Peter A.; Elliott, Henry L.;  
 Reid, John L.  
 AUTHOR(S):  
 CORPORATE SOURCE: Department Medicine and Therapeutics, Western Infirmary, Glasgow, G11 6NT, UK  
 SOURCE: Journal of Hypertension (1995), 13(12, Pt. 2), 1842-6  
 CODEN: JOHYD3; ISSN: 0263-6352  
 PUBLISHER: Current Science  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 IT 116644-53-2, Mibefradil  
 RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
 (hemodynamics, cardiac conduction and pharmacokinetics of mibefradil (Ro 40-5967), a novel calcium antagonist, in humans)  
 RN 116644-53-2 HCPLUS  
 CN Acetic acid, methoxy-, (1S,2S)-2-[2-[(3-(1H-benzimidazol-2-yl)propyl)methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl ester (9CI) (CA INDEX NAME)

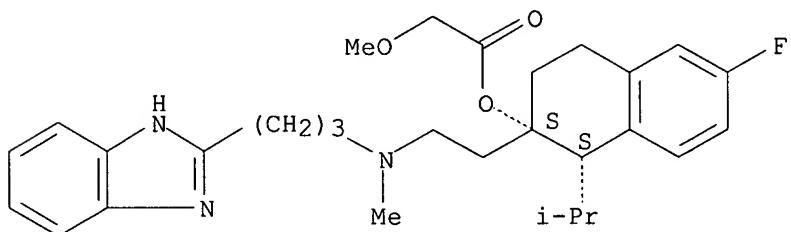
Absolute stereochemistry.



L41 ANSWER 404 OF 416 HCPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 1996:36342 HCPLUS  
 DOCUMENT NUMBER: 124:135217  
 TITLE: Effects of mibefradil on intracellular Ca2+ release in cultured rat cardiac fibroblasts and human platelets

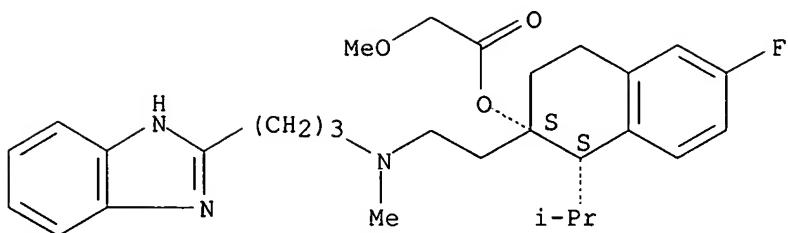
AUTHOR(S): Eberhard, Marc; Miyagawa, Koichi; Hermsmeyer, Kent;  
 Erne, Paul  
 CORPORATE SOURCE: Dep. Res., Kantonsspital, Basel, CH-4031, Switz.  
 SOURCE: Naunyn-Schmiedeberg's Archives of Pharmacology (1995),  
 353(1), 94-101  
 CODEN: NSAPCC; ISSN: 0028-1298  
 PUBLISHER: Springer  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 IT 116644-53-2, Mibefradil  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
 (mibefradil effect on calcium release in cardiac fibroblasts and human platelets)  
 RN 116644-53-2 HCPLUS  
 CN Acetic acid, methoxy-, (1S,2S)-2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



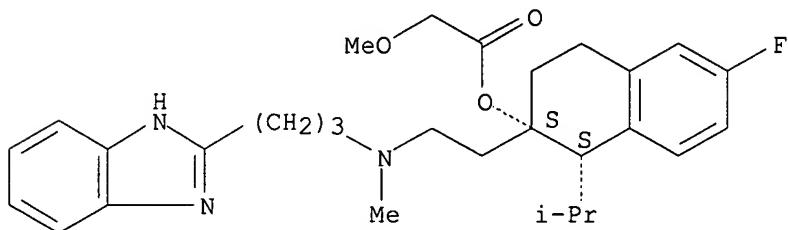
L41 ANSWER 405 OF 416 HCPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 1996:31775 HCPLUS  
 DOCUMENT NUMBER: 124:44687  
 TITLE: Nonlinear Pharmacokinetics of Mibefradil in the Dog  
 AUTHOR(S): Skerjanec, Andrej; Tawfik, Soheir; Tam, Yun K.  
 CORPORATE SOURCE: Faculty of Pharmacy and Pharmaceutical Sciences,  
 University of Alberta, Edmonton, AB, T6G 2N8, Can.  
 SOURCE: Journal of Pharmaceutical Sciences (1996), 85(2),  
 189-92  
 CODEN: JPMSAE; ISSN: 0022-3549  
 PUBLISHER: American Chemical Society  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 IT 116644-53-2, Mibefradil  
 RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
 (nonlinear pharmacokinetics of mibefradil in the dog)  
 RN 116644-53-2 HCPLUS  
 CN Acetic acid, methoxy-, (1S,2S)-2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L41 ANSWER 406 OF 416 HCAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 1996:29294 HCAPLUS  
 DOCUMENT NUMBER: 124:105447  
 TITLE: Two stable cell lines for screening of calcium channel blockers  
 AUTHOR(S): Seisenberger, Claudia; Welling, Andrea; Schuster, Angela; Hofmann, Franz  
 CORPORATE SOURCE: Inst. Pharmakologie und Toxikologie, TU Muenchen, Munich, D-80802, Germany  
 SOURCE: Naunyn-Schmiedeberg's Archives of Pharmacology (1995), 352(6), 662-9  
 CODEN: NSAPCC; ISSN: 0028-1298  
 PUBLISHER: Springer  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 IT 116644-53-2, Mibepradil  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
 (two stable cell lines for screening of calcium channel blockers)  
 RN 116644-53-2 HCAPLUS  
 CN Acetic acid, methoxy-, (1S,2S)-2-[2-[(3-(1H-benzimidazol-2-yl)propyl)methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L41 ANSWER 407 OF 416 HCAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 1996:28720 HCAPLUS  
 DOCUMENT NUMBER: 124:106113  
 TITLE: Mechanism of the antiischemic effect of mibepradil, a selective T calcium channel blocker in dogs: comparison with amlodipine  
 AUTHOR(S): Roux, Sebastien; Buehler, Manfred; Clozel, Jean-Paul  
 CORPORATE SOURCE: Pharma Division, F. Hoffmann-La Roche Ltd., Basel, CH-4002, Switz.  
 SOURCE: Journal of Cardiovascular Pharmacology (1996), 27(1), 132-9

CODEN: JCPCDT; ISSN: 0160-2446

PUBLISHER: Lippincott-Raven  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

IT 116644-53-2, Mibepradil

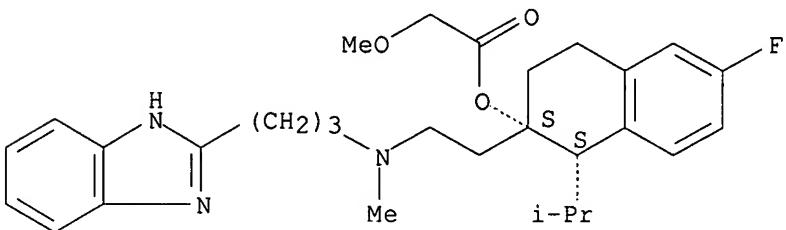
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(mechanism of the antiischemic effect of mibepradil, a selective T calcium channel blocker in dogs: comparison with amlodipine)

RN 116644-53-2 HCPLUS

CN Acetic acid, methoxy-, (1S,2S)-2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L41 ANSWER 408 OF 416 HCPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1995:941601 HCPLUS  
 DOCUMENT NUMBER: 124:52435

TITLE: Structural changes and cyclic GMP content of the aorta after calcium antagonism or angiotensin converting enzyme inhibition in renovascular hypertensive rats

AUTHOR(S): Veniant, Murielle; Gray, Gillian A.; Heudes, Didier; Menard, Joel; Clozel, Jean-Paul

CORPORATE SOURCE: Pharma Division, Preclinical Research, F. Hoffmann-La Roche Ltd, Basel, Switz.

SOURCE: Journal of Hypertension (1995), 13(7), 731-7  
 CODEN: JOHYD3; ISSN: 0263-6352

PUBLISHER: Current Science

DOCUMENT TYPE: Journal

LANGUAGE: English

IT 116644-53-2, Mibepradil

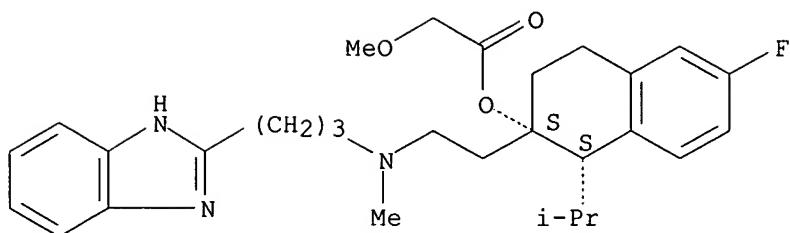
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(cGMP content and structural changes of aorta after calcium antagonism or angiotensin converting enzyme inhibition in renovascular hypertensive rats)

RN 116644-53-2 HCPLUS

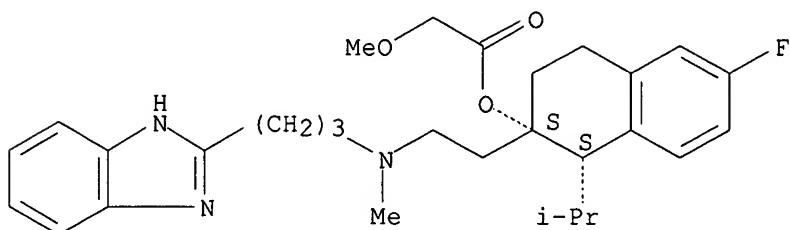
CN Acetic acid, methoxy-, (1S,2S)-2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L41 ANSWER 409 OF 416 HCPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 1995:911235 HCPLUS  
 DOCUMENT NUMBER: 124:21374  
 TITLE: Effects of the new calcium antagonist mibepradil (Ro 40-5967) on exercise duration in patients with chronic stable angina pectoris: A multicenter, placebo-controlled study  
 AUTHOR(S): Bakx, Ad L. M.; van der Wall, Ernst E.; Braun, Shimon; Emanuelsson, Hakan; Bruschke, Albert V. G.; Kobrin, Isaac  
 CORPORATE SOURCE: University Hospital, Leiden, Neth.  
 SOURCE: American Heart Journal (1995), 130(4), 748-57  
 CODEN: AHJOA2; ISSN: 0002-8703  
 PUBLISHER: Mosby-Year Book  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 IT 116644-53-2, Mibepradil  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (effects of the new calcium antagonist mibepradil (Ro 40-5967) on exercise duration in human patients with chronic stable angina pectoris)  
 RN 116644-53-2 HCPLUS  
 CN Acetic acid, methoxy-, (1S,2S)-2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L41 ANSWER 410 OF 416 HCPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 1995:865388 HCPLUS  
 DOCUMENT NUMBER: 123:329616  
 TITLE: The block of the expressed L-type calcium channel is modulated by the β3 subunit  
 AUTHOR(S): Lacinova, L.; Ludwig, A.; Bosse, E.; Flockerzi, V.; Hofmann, F.

CORPORATE SOURCE: Institut fuer Pharmakologie and Toxikologie TU  
Muenchen, Biedersteiner Str. 29, 80802, Munchen,  
Germany

SOURCE: FEBS Letters (1995), 373(2), 103-7  
CODEN: FEBLAL; ISSN: 0014-5793

PUBLISHER: Elsevier

DOCUMENT TYPE: Journal

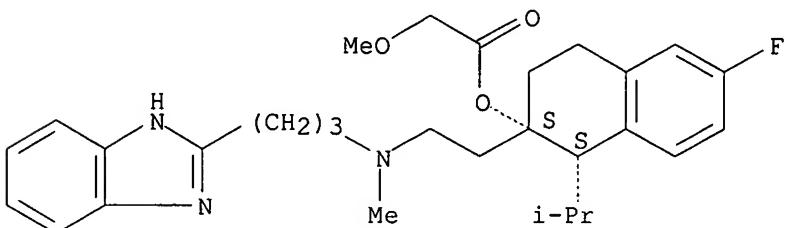
LANGUAGE: English

IT 116644-53-2, Mibepradil  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
(block of the expressed L-type calcium channel is modulated by the  $\beta 3$  subunit)

RN 116644-53-2 HCPLUS

CN Acetic acid, methoxy-, (1S,2S)-2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L41 ANSWER 411 OF 416 HCPLUS COPYRIGHT 2006 ACS on STN  
ACCESSION NUMBER: 1995:846309 HCPLUS  
DOCUMENT NUMBER: 123:275587  
TITLE: Voltage-dependent blockade of diverse types of voltage-gated  $\text{Ca}^{2+}$  channels expressed in *Xenopus* oocytes by the  $\text{Ca}^{2+}$  channel antagonist mibepradil (Ro 40-5967)

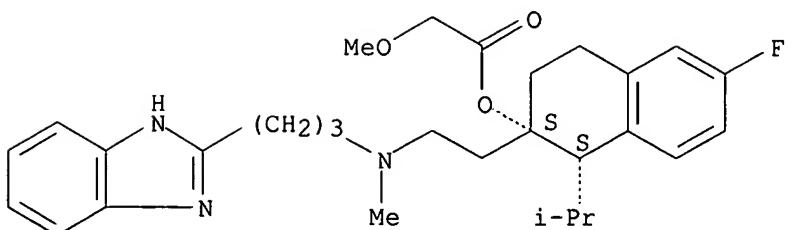
AUTHOR(S): Bezprozvanny, I.; Tsien, R. W.  
CORPORATE SOURCE: Dep. Mol. Cellular Physiology, Stanford University Medical Center, Stanford, CA, 94305, USA  
SOURCE: Molecular Pharmacology (1995), 48(3), 540-9  
CODEN: MOPMA3; ISSN: 0026-895X  
PUBLISHER: Williams & Wilkins  
DOCUMENT TYPE: Journal  
LANGUAGE: English

IT 116644-53-2, Mibepradil  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(voltage-dependent blockade of diverse types of voltage-gated  $\text{Ca}^{2+}$  channels expressed in *Xenopus* oocytes by mibepradil)

RN 116644-53-2 HCPLUS

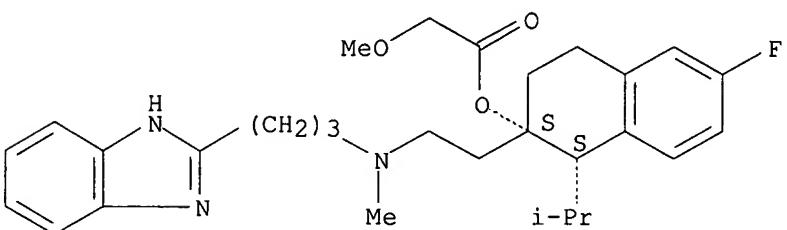
CN Acetic acid, methoxy-, (1S,2S)-2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L41 ANSWER 412 OF 416 HCPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 1995:755107 HCPLUS  
 DOCUMENT NUMBER: 123:188106  
 TITLE: Mibepradil prevents neointima formation after vascular injury in rats: possible role of the blockade of the T-type voltage-operated calcium channel  
 AUTHOR(S): Schmitt, R.; Clozel, J.-P.; Iberg, N.; Buehler, F. R.  
 CORPORATE SOURCE: Pharma Div., F. Hoffmann-La Roche Ltd., Basel, CH-4002, Switz.  
 SOURCE: Arteriosclerosis, Thrombosis, and Vascular Biology (1995), 15(8), 1161-5  
 CODEN: ATVBFA; ISSN: 1079-5642  
 PUBLISHER: American Heart Association  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 IT 116644-53-2, Mibepradil  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
 (role of calcium T-channels in blockade of injury-induced artery neointima formation by mibepradil)  
 RN 116644-53-2 HCPLUS  
 CN Acetic acid, methoxy-, (1S,2S)-2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L41 ANSWER 413 OF 416 HCPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 1995:719615 HCPLUS  
 DOCUMENT NUMBER: 123:132462  
 TITLE: Differential effects of the calcium antagonist mibepradil in epicardial and intramyocardial coronary arteries  
 AUTHOR(S): Kueng, Christoph F.; Tschudi, Marcel R.; Noll, Georg; Clozel, Jean-Paul; Luescher, Thomas F.  
 CORPORATE SOURCE: Department of Research, University Hospital, Basel, Switz.

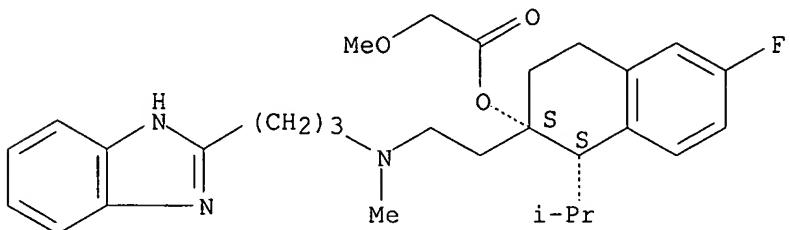
SOURCE: *Journal of Cardiovascular Pharmacology* (1995), 26(2), 312-18  
 CODEN: JCPCDT; ISSN: 0160-2446

PUBLISHER: Lippincott-Raven  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

IT 116644-53-2, Mibepradil  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (calcium antagonist mibepradil effects in epicardial and intramyocardial coronary arteries)

RN 116644-53-2 HCPLUS  
 CN Acetic acid, methoxy-, (1S,2S)-2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

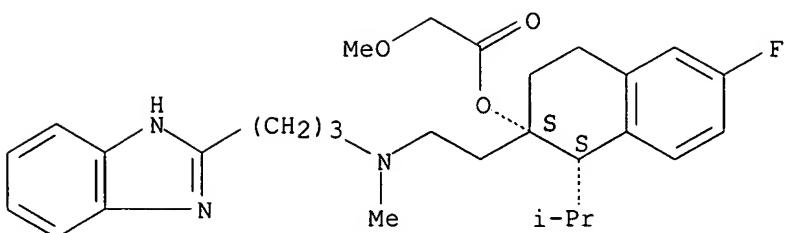


L41 ANSWER 414 OF 416 HCPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 1995:714882 HCPLUS  
 DOCUMENT NUMBER: 123:101913  
 TITLE: High-performance liquid chromatographic analysis of mibepradil in dog plasma and urine  
 AUTHOR(S): Skerjanec, A.; Tam, Y. K.  
 CORPORATE SOURCE: Faculty of Pharmacy and Pharmaceutical Sciences, University of Alberta, Edmonton, AB, T6G 2N8, Can.  
 SOURCE: Journal of Chromatography, B: Biomedical Applications (1995), 669(2), 377-82  
 CODEN: JCBBEP; ISSN: 0378-4347  
 PUBLISHER: Elsevier  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

IT 116644-53-2, Mibepradil  
 RL: ANT (Analyte); BPR (Biological process); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); PROC (Process)  
 (mibepradil determination in plasma and urine by HPLC)

RN 116644-53-2 HCPLUS  
 CN Acetic acid, methoxy-, (1S,2S)-2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L41 ANSWER 415 OF 416 HCPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1993:15784 HCPLUS

DOCUMENT NUMBER: 118:15784

TITLE: Metabolism of calcium antagonist Ro 40-5967: a case history of the use of diode-array UV spectroscopy and thermospray-mass spectrometry in the elucidation of a complex metabolic pathway

AUTHOR(S): Wiltshire, H. R.; Harris, S. R.; Prior, K. J.; Kozlowski, U. M.; Worth, E.

CORPORATE SOURCE: Dep. Pharmacokinet. Metab., Roche Prod. Ltd., Welwyn Garden City/Herts., AL7 3AY, UK

SOURCE: Xenobiotica (1992), 22(7), 837-57  
CODEN: XENOHB; ISSN: 0049-8254DOCUMENT TYPE: Journal  
LANGUAGE: English

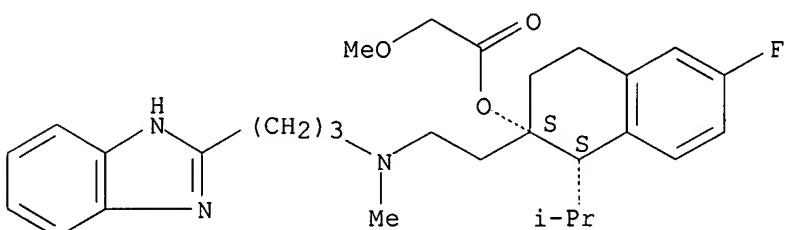
IT 116644-53-2

RL: PROC (Process)  
(as Ro 5967 metabolite, characterization of, by diode-array UV spectroscopy and thermospray-mass spectrometry)

RN 116644-53-2 HCPLUS

CN Acetic acid, methoxy-, (1S,2S)-2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L41 ANSWER 416 OF 416 HCPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1988:549535 HCPLUS

DOCUMENT NUMBER: 109:149535

TITLE: Preparation of [(heterocyclalkylamino)ethyl]tetrahydronaphthalenes as cardiovascular agents

INVENTOR(S): Branca, Quirico; Jaunin, Roland; Maerki, Hans Peter; Marti, Fraenzi; Ramuz, Henri

PATENT ASSIGNEE(S): Hoffmann-La Roche, F., und Co. A.-G., Switz.

SOURCE: Eur. Pat. Appl., 37 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: German  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 268148	A1	19880525	EP 1987-116251	19871104
EP 268148	B1	19911211		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
DK 8705599	A	19880515	DK 1987-5599	19871026
DK 171349	B1	19960916		
CA 1319144	A1	19930615	CA 1987-550190	19871026
CS 264350	B2	19890712	CS 1987-7874	19871103
AT 70267	E	19911215	AT 1987-116251	19871104
ES 2040234	T3	19931016	ES 1987-116251	19871104
ZA 8708362	A	19880727	ZA 1987-8362	19871106
AU 8780909	A1	19880519	AU 1987-80909	19871109
AU 600769	B2	19900823		
IL 84407	A1	19910916	IL 1987-84407	19871109
JP 63139171	A2	19880610	JP 1987-282287	19871110
JP 2504490	B2	19960605		
US 4808605	A	19890228	US 1987-119114	19871110
HU 60251	A2	19920828	HU 1987-5011	19871111
HU 215915	B	19990329		
FI 8705024	A	19880515	FI 1987-5024	19871113
FI 94414	B	19950531		
FI 94414	C	19950911		
NO 8704757	A	19880516	NO 1987-4757	19871113
NO 172237	B	19930315		
NO 172237	C	19930623		
CN 87107875	A	19880525	CN 1987-107875	19871113
CN 1028991	B	19950621		
PRIORITY APPLN. INFO.:			CH 1986-4565	A 19861114
			EP 1987-116251	A 19871104

OTHER SOURCE(S): MARPAT 109:149535

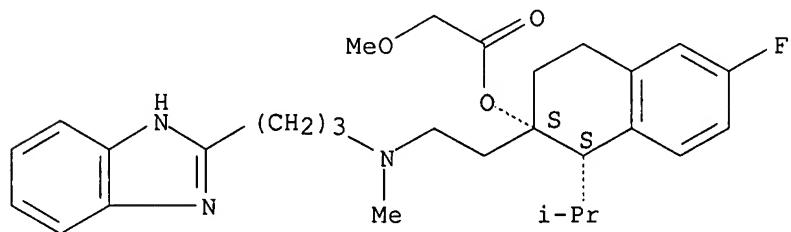
IT 116644-53-2P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (preparation of, as cardiovascular agent)

RN 116644-53-2 HCPLUS

CN Acetic acid, methoxy-, (1S,2S)-2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



=> d que stat 142  
 L38 1 SEA FILE=REGISTRY ABB=ON PLU=ON 116666-63-8  
 L42 63 SEA FILE=HCAPLUS ABB=ON PLU=ON L38

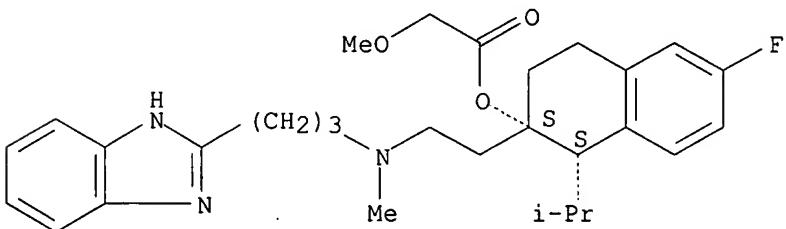
=> d 142 ibib hitstr 1-5 50-63

L42 ANSWER 1 OF 63 HCAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 2006:100738 HCAPLUS  
 DOCUMENT NUMBER: 144:198849  
 TITLE: Novel dosage form comprising modified-release and immediate-release active ingredients  
 INVENTOR(S): Vaya, Navin; Karan, Rajesh Singh; Sadanand, Sunil; Gupta, Vinod Kumar  
 PATENT ASSIGNEE(S): India  
 SOURCE: U.S. Pat. Appl. Publ., 49 pp., Cont.-in-part of U.S. Ser. No. 630,446.  
 CODEN: USXXCO  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2006024365	A1	20060202	US 2005-134633	20050519
US 2004096499	A1	20040520	US 2003-630446	20030729
PRIORITY APPLN. INFO.:				
			IN 2002-MU697	A 20020805
			IN 2002-MU699	A 20020805
			IN 2003-MU80	A 20030122
			IN 2003-MU82	A 20030122
			US 2003-630446	A2 20030729

IT 116666-63-8, Mibefradil dihydrochloride  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (novel dosage form comprising modified-release and immediate-release active ingredients)  
 RN 116666-63-8 HCAPLUS  
 CN Acetic acid, methoxy-, (1S,2S)-2-[2-[(3-(1H-benzimidazol-2-yl)propyl)methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl ester, dihydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

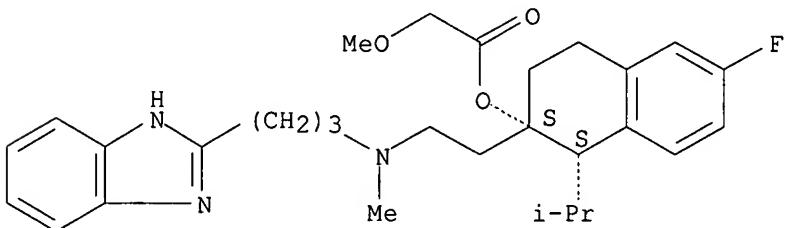


●2 HCl

L42 ANSWER 2 OF 63 HCAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 2005:1335082 HCAPLUS  
 DOCUMENT NUMBER: 144:57599  
 TITLE: Transdermal delivery system for statin combination therapy  
 INVENTOR(S): Lane, Edward M.  
 PATENT ASSIGNEE(S): Fairfield Clinical Trials, LLC, USA  
 SOURCE: U.S. Pat. Appl. Publ., 7 pp.  
 CODEN: USXXCO  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005281868	A1	20051222	US 2005-156744	20050621
WO 2006002127	A1	20060105	WO 2005-US21855	20050621
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
PRIORITY APPLN. INFO.:			US 2004-580734P	P 20040621
			US 2004-612828P	P 20040927
IT 116666-63-8, Posicor				
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)				
(transdermal delivery system for statin combination therapy of lipid disorders)				
RN 116666-63-8 HCAPLUS				
CN Acetic acid, methoxy-, (1S,2S)-2-[2-[(3-(1H-benzimidazol-2-yl)propyl)methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl ester, dihydrochloride (9CI) (CA INDEX NAME)				

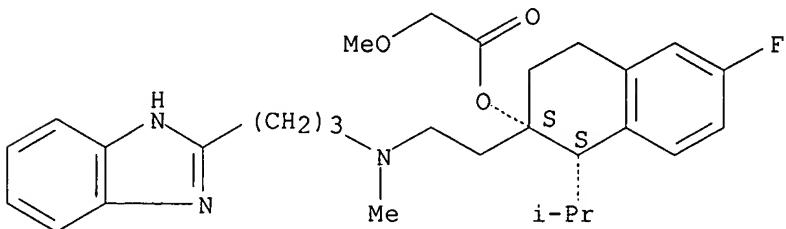
Absolute stereochemistry.



●2 HCl

L42 ANSWER 3 OF 63 HCAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 2005:388287 HCAPLUS  
 DOCUMENT NUMBER: 143:71181  
 TITLE: Modulation of Oral Squamous Cell Carcinoma Incidence  
 in Rats Via Diet and a Novel Calcium Channel  
 Antagonist  
 AUTHOR(S): Lenz, Barbara; Crameri, Flavio M.; Eichler, David A.;  
 Schlaeppi, Bernhard; Wiltshire, Hugh R.; Wood, John;  
 Seymour, Robin A.  
 CORPORATE SOURCE: Non-Clinical Development-Drug Safety, Hoffmann-La  
 Roche Ltd., Basel, Switz.  
 SOURCE: Toxicologic Pathology (2005), 33(3), 356-364  
 CODEN: TOPADD; ISSN: 0192-6233  
 PUBLISHER: Taylor & Francis, Inc.  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 IT 116666-63-8, Mibepradil dihydrochloride  
 RL: ADV (Adverse effect, including toxicity); DMA (Drug mechanism of  
 action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
 (Biological study); USES (Uses)  
 (mibepradil dihydrochloride showed dose dependent gingival overgrowth  
 in incisor and molar teeth independent of diet used, high-dose  
 administration raised incidence of periodontitis and squamous cell  
 carcinoma in rat)  
 RN 116666-63-8 HCAPLUS  
 CN Acetic acid, methoxy-, (1S,2S)-2-[2-[[3-(1H-benzimidazol-2-  
 yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-  
 2-naphthalenyl ester, dihydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



●2 HCl

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 4 OF 63 HCAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 2004:292562 HCAPLUS  
 DOCUMENT NUMBER: 140:399350  
 TITLE: NNC 55-0396 [(1S,2S)-2-(2-(N-[(3-benzimidazol-2-  
 yl)propyl]-N-methylamino)ethyl)-6-fluoro-1,2,3,4-  
 tetrahydro-1-isopropyl-2-naphthyl  
 cyclopropanecarboxylate dihydrochloride]: a new  
 selective inhibitor of T-type calcium channels  
 Huang, Luping; Keyser, Brian M.; Tagmose, Tina M.;  
 Hansen, J. Bondo; Taylor, James T.; Zhuang, Hean;  
 AUTHOR(S):

CORPORATE SOURCE: Zhang, Min; Ragsdale, David S.; Li, Ming  
 Department of Pharmacology, Tulane University Health Sciences Center, New Orleans, LA, USA

SOURCE: Journal of Pharmacology and Experimental Therapeutics (2004), 309(1), 193-199  
 CODEN: JPETAB; ISSN: 0022-3565

PUBLISHER: American Society for Pharmacology and Experimental Therapeutics

DOCUMENT TYPE: Journal

LANGUAGE: English

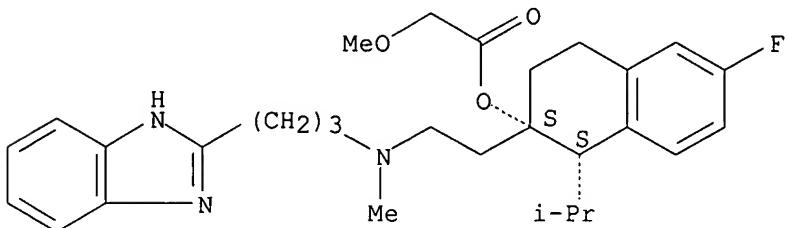
OTHER SOURCE(S): CASREACT 140:399350

IT 116666-63-8, Mibepradil dihydrochloride  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (mibepradil derivative selectively inhibits T-type calcium channels)

RN 116666-63-8 HCAPLUS

CN Acetic acid, methoxy-, (1S,2S)-2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl ester, dihydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



●2 HCl

REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 5 OF 63 HCAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 2001:916407 HCAPLUS  
 DOCUMENT NUMBER: 136:53755  
 TITLE: Synthesis of nitrosated and nitrosylated (hetero)cyclic phosphodiesterase inhibitors used in treatment of sexual dysfunction  
 INVENTOR(S): Garvey, David S.; Saenz de Tejada, Inigo; Earl, Richard A.; Khanapure, Subhash P.  
 PATENT ASSIGNEE(S): Nitromed, Inc., USA  
 SOURCE: U.S., 117 pp., Cont.-in-part of U.S. 5,958,926.  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 3  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6331543	B1	20011218	US 1999-387727	19990901
US 5874437	A	19990223	US 1996-740764	19961101

WO 9819672	A1	19980514	WO 1997-US19870	19971031
W: AU, CA, JP, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5958926	A	19990928	US 1998-145142	19980901
US 2002019405	A1	20020214	US 2001-941691	20010830
US 6462044	B2	20021008		
US 2003023087	A1	20030130	US 2002-216886	20020813
US 6930113	B2	20050816		
US 2004087591	A1	20040506	US 2003-694183	20031028
PRIORITY APPLN. INFO.:			US 1996-740764	A2 19961101
			WO 1997-US19870	A2 19971031
			US 1998-145142	A2 19980901
			US 1999-387727	A1 19990901
			US 2001-941691	A3 20010830
			US 2002-216866	A3 20020813

OTHER SOURCE(S): MARPAT 136:53755

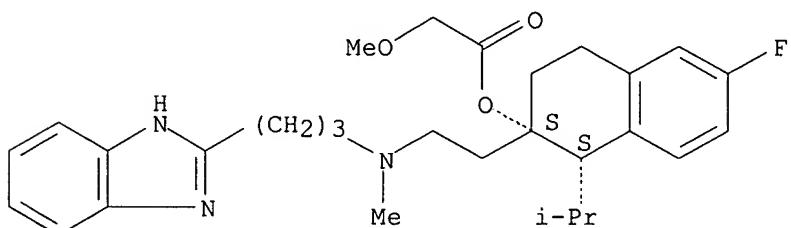
IT 116666-63-8D, Posicor, nitroso derivs.

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(synthesis of nitrosated and nitrosylated (hetero)cyclic phosphodiesterase inhibitors used in treatment of sexual dysfunction)

RN 116666-63-8 HCPLUS

CN Acetic acid, methoxy-, (1S,2S)-2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl ester, dihydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



●2 HCl

REFERENCE COUNT: 86 THERE ARE 86 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 50 OF 63 HCPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1993:204998 HCPLUS

DOCUMENT NUMBER: 118:204998

TITLE: Effects of Ro 40-5967, a new calcium antagonist, and enalapril on cardiac remodeling in renal hypertensive rats

AUTHOR(S): Veniant, Murielle; Clozel, Jean Paul; Heudes, Didier; Banken, Ludger; Menard, Joel

CORPORATE SOURCE: Pharma Div., F. Hoffmann-La Roche, Basel, CH-4002, Switz.

SOURCE: Journal of Cardiovascular Pharmacology (1993), 21(4), 544-51

CODEN: JCPCDT; ISSN: 0160-2446

DOCUMENT TYPE: Journal  
 LANGUAGE: English

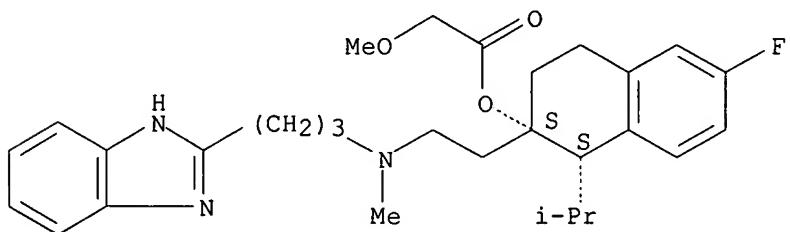
IT 116666-63-8

RL: BIOL (Biological study)  
 (cardiac remodeling in renal hypertension response to enalapril vs.)

RN 116666-63-8 HCAPLUS

CN Acetic acid, methoxy-, (1S,2S)-2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl ester, dihydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



●2 HCl

L42 ANSWER 51 OF 63 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1993:139549 HCAPLUS

DOCUMENT NUMBER: 118:139549

TITLE: Ro 40-5967, a novel calcium channel antagonist,  
 protects against ventricular fibrillation

AUTHOR(S): Billman, George E.

CORPORATE SOURCE: Dep. Physiol., Ohio State Univ., Columbus, OH, USA

SOURCE: European Journal of Pharmacology (1993), 229(2-3),  
 179-87

CODEN: EJPHAZ; ISSN: 0014-2999

DOCUMENT TYPE: Journal

LANGUAGE: English

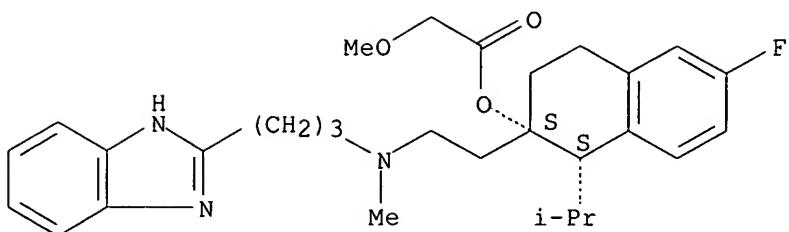
IT 116666-63-8

RL: PRP (Properties)  
 (antiarrhythmic effects of, in heart ischemia and ventricular  
 fibrillation)

RN 116666-63-8 HCAPLUS

CN Acetic acid, methoxy-, (1S,2S)-2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl ester, dihydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



●2 HCl

L42 ANSWER 52 OF 63 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1993:15784 HCAPLUS

DOCUMENT NUMBER: 118:15784

TITLE: Metabolism of calcium antagonist Ro 40-5967: a case history of the use of diode-array UV spectroscopy and thermospray-mass spectrometry in the elucidation of a complex metabolic pathway

AUTHOR(S): Wiltshire, H. R.; Harris, S. R.; Prior, K. J.; Kozlowski, U. M.; Worth, E.

CORPORATE SOURCE: Dep. Pharmacokinet. Metab., Roche Prod. Ltd., Welwyn Garden City/Herts., AL7 3AY, UK

SOURCE: Xenobiotica (1992), 22(7), 837-57  
CODEN: XENOHB; ISSN: 0049-8254

DOCUMENT TYPE: Journal  
LANGUAGE: English

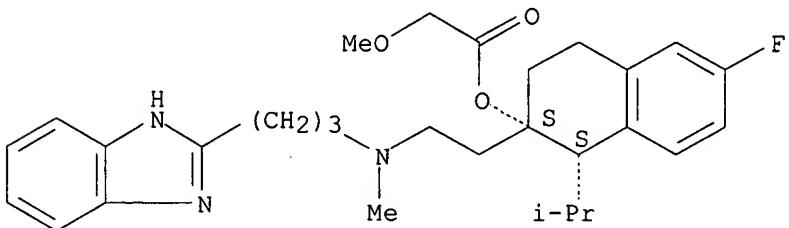
IT 116666-63-8

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(metabolism of, diode-array UV spectroscopy and thermospray-mass spectrometry in elucidation of complex metabolic pathway in)

RN 116666-63-8 HCAPLUS

CN Acetic acid, methoxy-, (1S,2S)-2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl ester, dihydrochloride (9CI) (CA INDEX NAME)

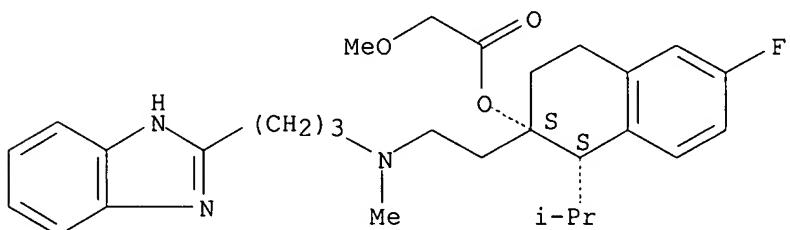
Absolute stereochemistry.



●2 HCl

L42 ANSWER 53 OF 63 HCAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 1992:604926 HCAPLUS  
 DOCUMENT NUMBER: 117:204926  
 TITLE: Effect of calcium channel antagonists on the cardiac vagal tone response to submaximal exercise  
 AUTHOR(S): Billman, George E.; Halliwill, John R.; Avendano, Christopher E.  
 CORPORATE SOURCE: Dep. Physiol., Ohio State Univ., Columbus, OH, USA  
 SOURCE: Drug Development Research (1992), 27(2), 89-106  
 CODEN: DDREDK; ISSN: 0272-4391  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 IT 116666-63-8  
 RL: BIOL (Biological study)  
 (exercise effect on cardiac vagal tone response to, as calcium channel antagonist)  
 RN 116666-63-8 HCAPLUS  
 CN Acetic acid, methoxy-, (1S,2S)-2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl ester, dihydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

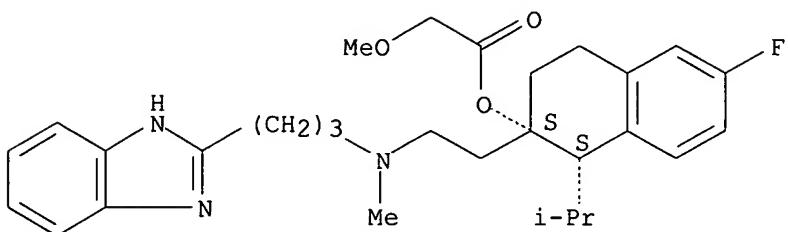


●2 HCl

L42 ANSWER 54 OF 63 HCAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 1992:143594 HCAPLUS  
 DOCUMENT NUMBER: 116:143594  
 TITLE: Hemodynamic profile of Ro 40-5967 in conscious rats: comparison with diltiazem, verapamil, and amlodipine  
 AUTHOR(S): Veniant, Murielle; Clozel, Jean Paul; Hess, Patrick; Wolfgang, Robert  
 CORPORATE SOURCE: Pharma Div., F. Hoffmann-La Roche Ltd., Basel, CH-4002, Switz.  
 SOURCE: Journal of Cardiovascular Pharmacology (1991), 18(Suppl. 10), S55-S58  
 CODEN: JCPCDT; ISSN: 0160-2446  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 IT 116666-63-8  
 RL: BIOL (Biological study)  
 (hemodynamic profile of, as calcium antagonist)  
 RN 116666-63-8 HCAPLUS  
 CN Acetic acid, methoxy-, (1S,2S)-2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-

2-naphthalenyl ester, dihydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



●2 HCl

L42 ANSWER 55 OF 63 HCPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1992:33723 HCPLUS

DOCUMENT NUMBER: 116:33723

TITLE: Ro 40-5967: a new nondihydropyridine calcium antagonist

AUTHOR(S): Clozel, Jean Paul; Osterrieder, Wolfgang; Kleinbloesem, Cornelis H.; Welker, Horst A.; Schlaeppi, Bernhard; Tudor, Robert; Hefti, Fridolin; Schmitt, Rita; Eggers, Herwig

CORPORATE SOURCE: Pharm. Res. Dep., F. Hoffmann-La Roche Ltd., Basel, CH-4002, Switz.

SOURCE: Cardiovascular Drug Reviews (1991), 9(1), 4-17

DOCUMENT TYPE: CODEN: CDREEA; ISSN: 0897-5957

LANGUAGE: English

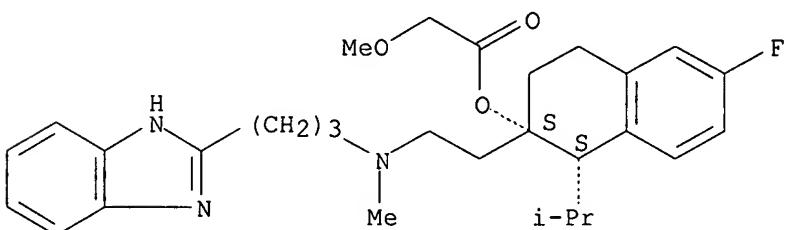
IT 116666-63-8

RL: BIOL (Biological study)  
(as nondihydropyridine calcium antagonist)

RN 116666-63-8 HCPLUS

CN Acetic acid, methoxy-, (1S,2S)-2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl ester, dihydrochloride (9CI) (CA INDEX NAME)

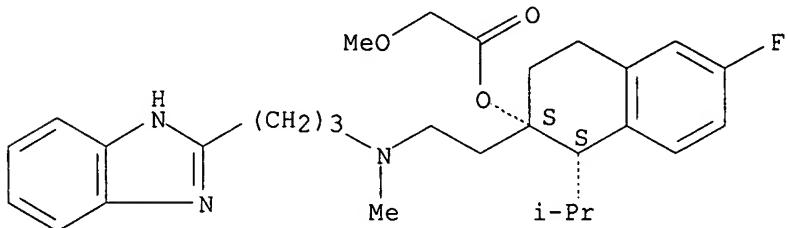
Absolute stereochemistry.



●2 HCl

L42 ANSWER 56 OF 63 HCPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 1991:240328 HCPLUS  
 DOCUMENT NUMBER: 114:240328  
 TITLE: Potential-dependent inhibition of cardiac calcium inward currents by Ro 40-5967 and verapamil: relation to negative inotropy  
 AUTHOR(S): Fang, Liang Min; Osterrieder, Wolfgang  
 CORPORATE SOURCE: Pharm. Res. Dep., F. Hoffmann-La Roche Ltd., Basel, CH-4002, Switz.  
 SOURCE: European Journal of Pharmacology (1991), 196(2), 205-7  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 IT 116666-63-8  
 RL: BIOL (Biological study)  
 (heart calcium currents and neg. inotropic response to)  
 RN 116666-63-8 HCPLUS  
 CN Acetic acid, methoxy-, (1S,2S)-2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl ester, dihydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

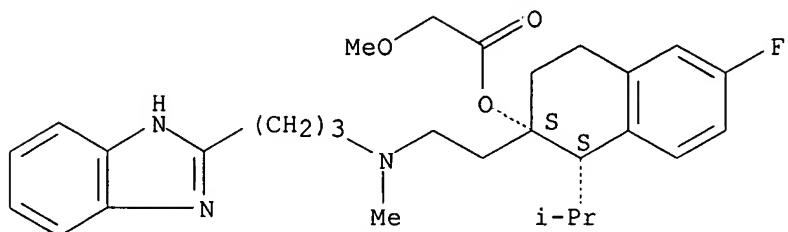


●2 HCl

L42 ANSWER 57 OF 63 HCPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 1991:240319 HCPLUS  
 DOCUMENT NUMBER: 114:240319  
 TITLE: Increased negative inotropic effect of calcium-channel blockers in hypertrophied and failing rabbit heart  
 AUTHOR(S): Ezzaher, Abdellatif; Bouanani, Nour el Houda; Su, Jin Bo; Hittinger, Luc; Crozatier, Bertrand  
 CORPORATE SOURCE: Fac. Med., Hop. Henri Mondor, Creteil, 94000, Fr.  
 SOURCE: Journal of Pharmacology and Experimental Therapeutics (1991), 257(1), 466-71  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 IT 116666-63-8  
 RL: PRP (Properties)  
 (increased neg. inotropic effect of, in heart failure and hypertrophy)  
 RN 116666-63-8 HCPLUS  
 CN Acetic acid, methoxy-, (1S,2S)-2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-

2-naphthalenyl ester, dihydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



●2 HCl

L42 ANSWER 58 OF 63 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1991:94918 HCAPLUS

DOCUMENT NUMBER: 114:94918

TITLE: Ro 40-5967, in contrast to diltiazem, does not reduce left ventricular contractility in rats with chronic myocardial infarction

AUTHOR(S): Veniant, Murielle; Clozel, Jean Paul; Hess, Patrick; Wolfgang, Robert

CORPORATE SOURCE: Pharm. Res. Dep., F. Hoffmann-La Roche Ltd., Basel, CH-4002, Switz.

SOURCE: Journal of Cardiovascular Pharmacology (1991), 17(2), 277-84

CODEN: JCPCDT; ISSN: 0160-2446

DOCUMENT TYPE: Journal

LANGUAGE: English

IT 116666-63-8, Ro 40-5967

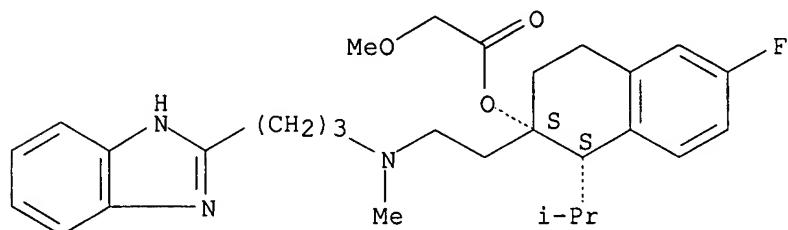
RL: PRP (Properties)

(neg. inotropic effect of, in heart infarction)

RN 116666-63-8 HCAPLUS

CN Acetic acid, methoxy-, (1S,2S)-2-[2-[(3-(1H-benzimidazol-2-yl)propyl)methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl ester, dihydrochloride (9CI) (CA INDEX NAME)

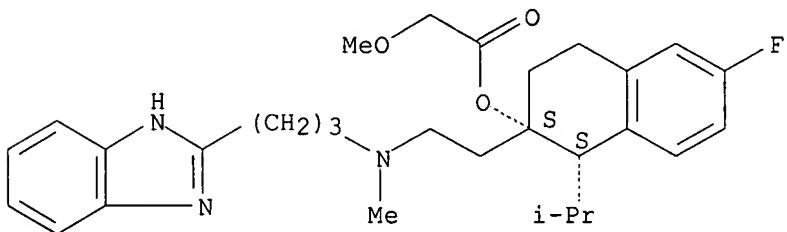
Absolute stereochemistry.



●2 HCl

L42 ANSWER 59 OF 63 HCPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 1990:609229 HCPLUS  
 DOCUMENT NUMBER: 113:209229  
 TITLE: The proliferative response to vascular injury is suppressed by angiotensin-converting enzyme inhibition  
 AUTHOR(S): Powell, Jerry S.; Mueller, Rita K. M.; Rouge, Marianne; Kuhn, Herbert; Hefti, Fridolin; Baumgartner, Hans R.  
 CORPORATE SOURCE: F. Hoffmann-La Roche Ltd., Basel, Switz.  
 SOURCE: Journal of Cardiovascular Pharmacology (1990), 16(Suppl. 4), S42-S49  
 CODEN: JCPCTD; ISSN: 0160-2446  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 IT 116666-63-8  
 RL: BIOL (Biological study)  
 (blood vessel proliferation response to, angiotensin-converting enzyme inhibition in relation to)  
 RN 116666-63-8 HCPLUS  
 CN Acetic acid, methoxy-, (1S,2S)-2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl ester, dihydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



●2 HCl

L42 ANSWER 60 OF 63 HCPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 1990:229520 HCPLUS  
 DOCUMENT NUMBER: 112:229520  
 TITLE: Antihypertensive properties of the novel calcium antagonist (1S,2S)-2-[2-[[3-(2-benzimidazolyl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-isopropyl-2-naphthyl methoxyacetate dihydrochloride in rat models of hypertension. Comparison with verapamil  
 AUTHOR(S): Hefti, F.; Clozel, J. P.; Osterrieder, W.  
 CORPORATE SOURCE: F. Hoffmann-La Roche Ltd., Basel, Switz.  
 SOURCE: Arzneimittel-Forschung (1990), 40(4), 417-21  
 CODEN: ARZNAD; ISSN: 0004-4172  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 IT 116666-63-8  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological

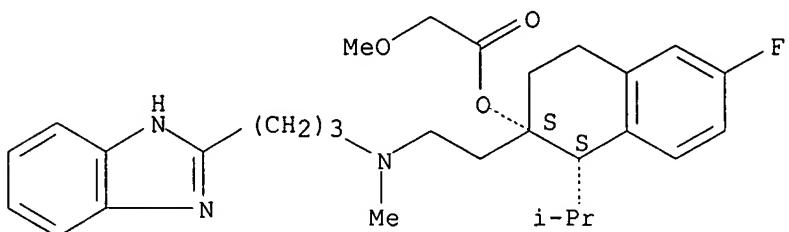
study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(antihypertensive activity of)

RN 116666-63-8 HCPLUS

CN Acetic acid, methoxy-, (1S,2S)-2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl ester, dihydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



●2 HCl

L42 ANSWER 61 OF 63 HCPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1989:625064 HCPLUS

DOCUMENT NUMBER: 111:225064

TITLE: Effects of Ro 40-5967, a novel calcium antagonist, on myocardial function during ischemia induced by lowering coronary perfusion pressure in dogs: comparison with verapamil

AUTHOR(S): Clozel, Jean Paul; Banken, Ludger; Osterrieder, Wolfgang

CORPORATE SOURCE: Pharm. Res. Dep., F. Hoffmann-La Roche and Co., Ltd., Basel, CH-4002, Switz.

SOURCE: Journal of Cardiovascular Pharmacology (1989), 14(5), 713-21

CODEN: JCPCDT; ISSN: 0160-2446

DOCUMENT TYPE: Journal

LANGUAGE: English

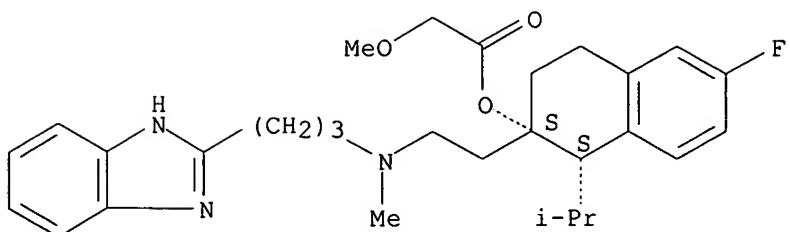
IT 116666-63-8, Ro 40-5967

RL: BIOL (Biological study)  
(heart ischemia inhibition by)

RN 116666-63-8 HCPLUS

CN Acetic acid, methoxy-, (1S,2S)-2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl ester, dihydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



●2 HCl

L42 ANSWER 62 OF 63 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1989:400442 HCAPLUS

DOCUMENT NUMBER: 111:442

TITLE: In vitro pharmacologic profile of Ro 40-5967, a novel calcium channel blocker with potent vasodilator but weak inotropic action

AUTHOR(S): Osterrieder, Wolfgang; Holck, Mark

CORPORATE SOURCE: Pharm. Res. Dep., F. Hoffmann-La Roche and Co., Ltd., Basel, CH-4002, Switz.

SOURCE: Journal of Cardiovascular Pharmacology (1989), 13(5), 754-9

DOCUMENT TYPE: CODEN: JCPCDT; ISSN: 0160-2446

Journal

LANGUAGE: English

IT 116666-63-8, Ro 40-5967

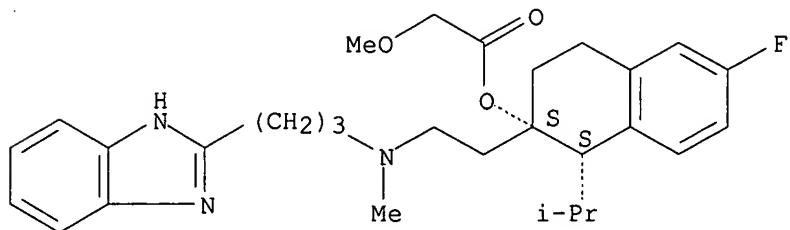
RL: BIOL (Biological study)

(coronary artery dilation by, inotropic action in relation to)

RN 116666-63-8 HCAPLUS

CN Acetic acid, methoxy-, (1S,2S)-2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl ester, dihydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



●2 HCl

L42 ANSWER 63 OF 63 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1988:549535 HCAPLUS

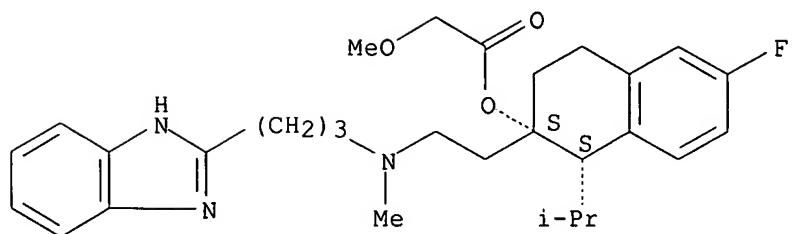
DOCUMENT NUMBER: 109:149535

TITLE: Preparation of [[(heterocyclylalkyl)amino]ethyl]tetrahydronaphthalenes as cardiovascular agents  
 INVENTOR(S): Branca, Quirico; Jaunin, Roland; Maerkli, Hans Peter;  
 Marti, Fraenzi; Ramuz, Henri  
 PATENT ASSIGNEE(S): Hoffmann-La Roche, F., und Co. A.-G., Switz.  
 SOURCE: Eur. Pat. Appl., 37 pp.  
 CODEN: EPXXDW  
 DOCUMENT TYPE: Patent  
 LANGUAGE: German  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 268148	A1	19880525	EP 1987-116251	19871104
EP 268148	B1	19911211		
R: AT, BE, CH, DK 8705599	DE, ES, FR, GB, GR, IT, LI, LU, NL, SE	19980515	DK 1987-5599	19871026
DK 171349	B1	19960916		
CA 1319144	A1	19930615	CA 1987-550190	19871026
CS 264350	B2	19890712	CS 1987-7874	19871103
AT 70267	E	19911215	AT 1987-116251	19871104
ES 2040234	T3	19931016	ES 1987-116251	19871104
ZA 8708362	A	19880727	ZA 1987-8362	19871106
AU 8780909	A1	19880519	AU 1987-80909	19871109
AU 600769	B2	19900823		
IL 84407	A1	19910916	IL 1987-84407	19871109
JP 63139171	A2	19880610	JP 1987-282287	19871110
JP 2504490	B2	19960605		
US 4808605	A	19890228	US 1987-119114	19871110
HU 60251	A2	19920828	HU 1987-5011	19871111
HU 215915	B	19990329		
FI 8705024	A	19880515	FI 1987-5024	19871113
FI 94414	B	19950531		
FI 94414	C	19950911		
NO 8704757	A	19880516	NO 1987-4757	19871113
NO 172237	B	19930315		
NO 172237	C	19930623		
CN 87107875	A	19880525	CN 1987-107875	19871113
CN 1028991	B	19950621		
PRIORITY APPLN. INFO.:			CH 1986-4565	A 19861114
			EP 1987-116251	A 19871104

OTHER SOURCE(S): MARPAT 109:149535  
 IT 116666-63-8P  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (preparation of, as cardiovascular agent)  
 RN 116666-63-8 HCPLUS  
 CN Acetic acid, methoxy-, (1S,2S)-2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl ester, dihydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



●2 HCl